VOLUME 29 JULY 1936 NUMBER 7

Southern Medical Journal

Journal of the Southern Medical Association

Copyright, Southern Medical Association, 1936. Published monthly by the Southern Medical Association, Empire Building, Birmingham, Alabama. Annual subscription $4.00. Entered as Second-Class Matter at the Post Office at Birmingham, Alabama, under Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of October 3, 1917, authorized December 20, 1921.

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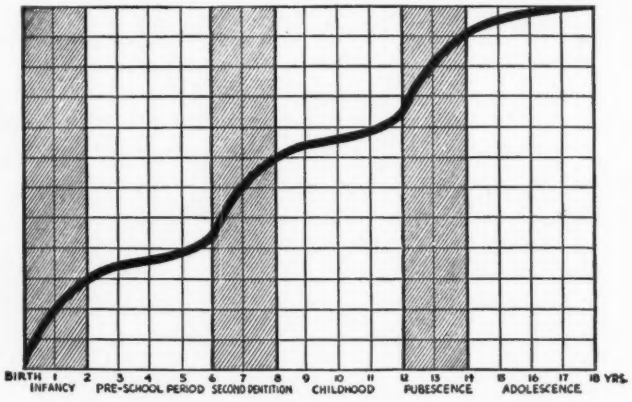

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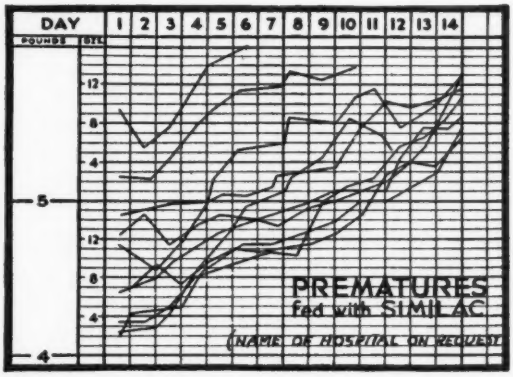

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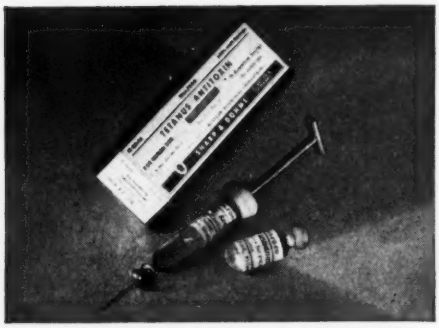

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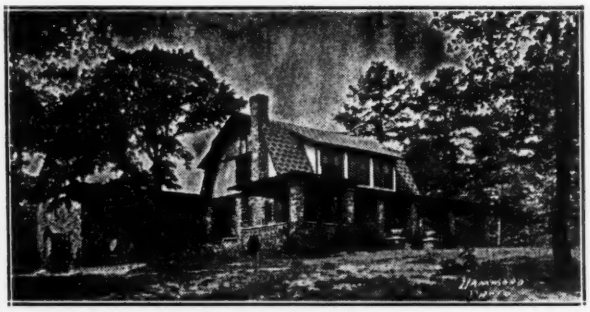

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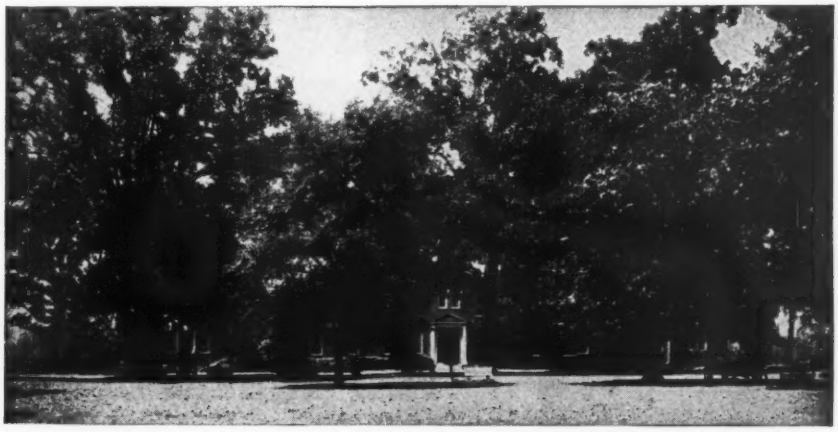

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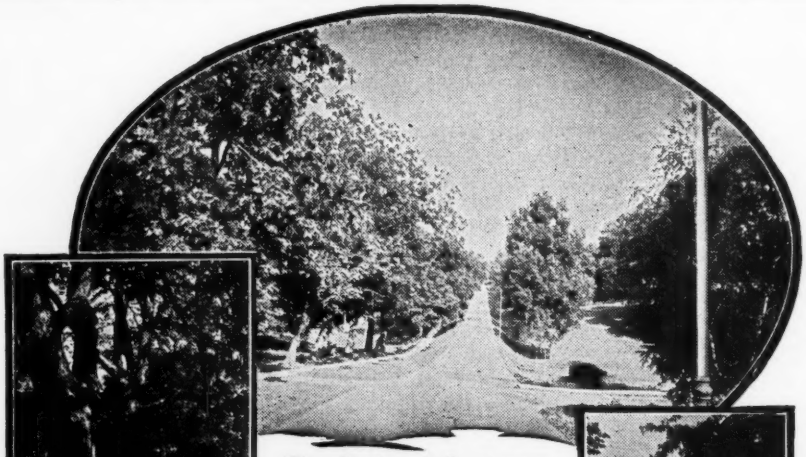

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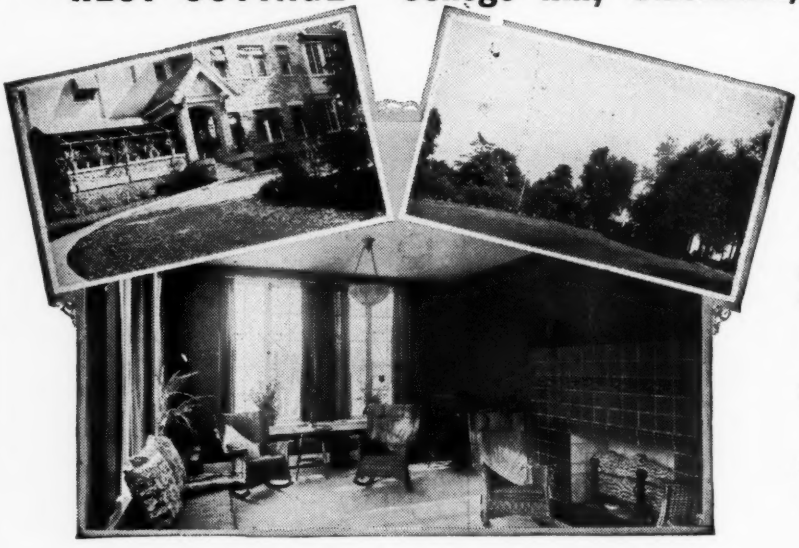

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Volume 29 JULY 1936 Number 7

PREOPERATIVE IRRADIATION OF BREAST TUMORS*

By JOSEPH COLT BLOODGOOD, M.D.†
and
GEORGE A. STEWART, M.D.
Baltimore, Md.

Introduction by Dr. Stewart.—It seems unnecessary to say very much of Dr. Bloodgood's achievements in the field of surgery and surgical pathology to such a group of men as I see before me. Of the twelve men who have presented, and will present, papers in this section of the Southern Medical Association today, seven are men who were either his students or residents, or who worked in his laboratory with him. This would have been a great source of satisfaction and pleasure to him had he seen the program of today's meeting. Many of you knew him personally, all of you knew him through his work in cancer and cancer prevention.

While he had been in poor health for some time, he had been coming to his office daily, seeing patients and attending to his correspondence. On October 22, while with his family in his home, he suddenly collapsed and died before Dr. Cohn or I could reach him.

In his death, we who have been closely associated with him so long have lost our friend, our leader, our inspiration. The nation has lost a great crusader in the cause of prevention and cure of cancer, a pioneer in many phases of cancer work.

He began his fight in 1893, and laid it down at his death, forty-two years of tireless devotion to the cause which was his very thought and life. His command to us was to carry on no matter what the cost, no matter how hopeless the task might appear.

May we never forget his aims and his unselfish devotion to his set purpose, and may we be worthy followers in the path he laid down with such care, study, and unceasing labor.

It is, therefore, with a deep sense of gratitude and may I add reverence that I read this last completed paper. It has not been changed since his death. Although Dr. Cohn and I collaborated with him in its preparation, the "I" is always Dr. Bloodgood himself, and it is of him that I wish you to think as I read it, a task which, although difficult for me to do, I am glad to do, as it was his last request of me.

TUMORS CLINICALLY MALIGNANT TO BE TREATED BY IRRADIATION, FOLLOWED BY OPERATION; THOSE CLINICALLY BENIGN TO BE DIAGNOSED BY ASPIRATION OR BIOPSY, OR EXCISION OF THE CLINICALLY BENIGN TUMOR

The first case which I subjected to preoperative irradiation was J. C. B., 24493, Pathol. No. 53502. The patient was first seen by Dr. Cohn and me on June 8, 1934. The palpable lump in the breast showed certain changes which were diagnosed by us as malignant. Without preliminary biopsy, the patient was treated by irradiation with radium by Dr. Curtis F. Burnam at the Kelly Hospital. The complete operation for cancer was performed September 13, 1934, three months after the beginning of the irradiation. The culture of the tissue removed at this operation showed a definite growth of living cells, but the lymph nodes, on microscopic examination, showed no involvement. This patient (Mrs. E.) is living today, September 28, 1935, and free from recurrence.

Among the three cases now before me, this is the only one in which there was a definite growth of the tissues on culture. (Our experience with tissue growth on culture *in vitro* will later on be made the subject of another article.) In the other two cases of early cancer, the lesions were irradiated, one after aspiration biopsy and one without biopsy, the complete operation following later in both instances. The axillary glands were not involved. Tissue obtained at these operations and placed in culture failed to grow. These two patients are also living.

Apparently we have sufficient evidence to

*Read in Section on Surgery, Southern Medical Association, Twenty-Ninth Annual Meeting, St. Louis, Missouri, November 19-22, 1935.

†Died October 22, 1935.

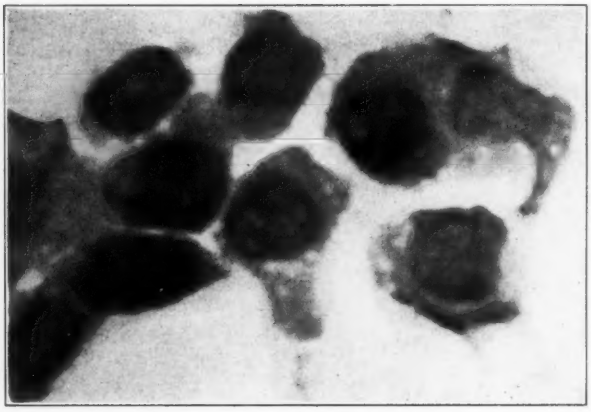

Fig. 1
Path. No. 55348. Shows cancer cells from aspiration biopsy of tumor of breast before irradiation.

demonstrate that the moment irradiation of a cancer of the breast and its metastatic area is begun, there is no further growth of cancer cells in the cancer nodule and in the metastatic nodule.

The details of the last case are as follows:

Mrs. S. (Pathol. No. 55348) was seen by Drs. Stewart, Cohn and myself June 17, 1935, with a lump in the mid-zone of the lower and outer quadrant of the left breast; the palpable tumor was smaller than a twenty-five-cent piece. It did not fluctuate, nor did it feel spherical like a cyst, but like a solid tumor of irregular outline. For this reason the patient was admitted to the hospital and prepared for aspiration or biopsy, but not for the complete excision which was not contemplated unless the tumor proved to be benign. After the breast was properly cleaned up, it was aspirated by Dr. Cohn, but all the material that could be obtained did not fill the aspirating needle. This material was stained and, on microscopic examination, contained a group of cancer cells (*Fig. 1*). The patient was immediately referred to Dr. Burnam and given a complete course of irradiation with deep x-rays over a period from June 18 to July 3, 1935. During this time practically all of the palpable mass disappeared. On August 5, on transillumination by Dr. Cohn, the area which had been distinctly dark when transilluminated June 17 (before irradiation) was now only slightly darker; the irritation of the skin had about subsided. It was considered wiser to wait until September 18, when the patient was re-examined by Dr. Cohn at the office. There were no signs whatever of irritation of the skin and nothing on transillumination and palpation. The complete operation was done September 18, 1935. At this time, after considerable search, we could find in the region of the palpable tumor an area of gross typical cancer. *Fig. 2* is a photomicrograph of this area. There was no evidence of cancer in any of the lymph nodes removed, nor was there any evidence of growth in the aspirated cancerous nodule after irradiation had begun. In fact, it was smaller three months later when removed than at the time of the aspiration.

This is our latest case of cancer of the breast subjected to preoperative irradiation, followed three months later by the complete operation for cancer. There was no growth on tissue culture.

We have just started irradiation preliminary to operation on a new case which is clinically malignant, sufficiently doubtful on transillumination to suggest malignancy, but without palpable lymph nodes in the axilla.

Dr. Burnam is now using deep x-rays for the preoperative irradiation of breast tumors when they are small and operable, reserving radium for irradiation and implantation in later cases.

My experience, since my first successful case of preoperative irradiation of an apparently inoperable and hopeless case, dates back to June, 1932. This patient is still living after irradiation by Dr. Kelly and his son by means of radium packs and the implantation of radon

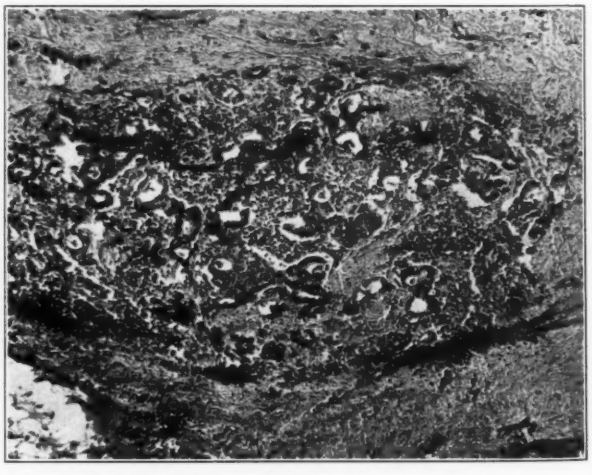

Fig. 2
Path. No. 55348. Area of breast showing cancer cells after irradiation and complete operation for cancer. No cultural growth of cells.

seeds, followed, after a delay of about three months, by the excision of the mass in the chest wall with the actual cautery; nothing further was done. This patient is clinically well today. This case was reported with illustrations in the *American Journal of Surgery* (New Series, 28:490-497). I made my first report in the *Annals of Surgery* (November, 1932, p. 882) and in *Radiology* (22:651-656, June, 1934). It is less than four years since I have taken up preoperative irradiation, but I feel convinced of its value.

In the *Nova Scotia Medical Bulletin* for March, 1935 (16:126), I made such an important statement in regard to the attitude of the medical profession towards lumps in the breast that I wish to repeat it here and to incorporate with it the statement made before a Chautauqua audience on July 24, 1935, and reported in the *Chautauqua Daily Journal* of July 25, 1935.

In the *Nova Scotia Medical Journal* I brought out for the first time in very emphatic form that I felt that every woman would be warned in time by a lump in the breast or some other sign or symptom of a possible dangerous lesion in the breast, but that the difficulty would be to get her to act in time. Every woman should act within two weeks after the first warning. The breast should be examined by a physician, and, if there is the slightest sign or suspicion of cancer, irradiation with x-rays or radium should be begun at once, because, the moment irradiation of the breast lesion begins, danger of further delay stops. This danger of delay after two weeks is not yet appreciated by the women themselves and by many members of the medical profession. The danger of delay is that the palpable lump, or the first warning of any kind of a lesion of the breast, may be that of a malignant tumor. In a further delay of two weeks metastasis to the neighboring lymph nodes may take place and reduce the chances of a permanent cure to 25 per cent. So that the moment anything suggestive of malignancy is found in the breast irradiation with x-rays or radium by a properly qualified radiotherapeutist should begin at once.

It is this time element that is not yet appreciated by women and many members of the medical profession and makes a lump in the breast a dangerous thing. In the first two weeks it may be dangerous to 5 or 10 per cent of the women. When women are instructed to report for examination within two weeks and all receive proper irradiation whenever there is any sign of malignancy, the danger of cancer of the breast will become more and more insignificant.

As women increase their vigilance and take immediate action in relation to conditions in the breast, they will begin to lose their fear, because they will know that, in addition to surgery, they will have the benefits of treatment by irradiation with x-rays and radium.

DISCUSSION (*Abstract*)

Dr. Frank K. Boland, Atlanta, Ga.—A good many years ago, when preoperative irradiation of malignant breast tumors was first proposed, I tried the procedure in three cases, was disappointed in the results, and abandoned it. These cases all had involvement of the lymph nodes and may have had thoracic involvement as well, but we were not x-raying the chest in those days for metastasis. Two of the patients survived about the usual length of time in such cases, one or two years, and the third and last one died within one month after radical excision of the tumor and lymph nodes. Apparently the operations were done thoroughly, but it probably is true that irradiation twenty years ago was very imperfectly applied. We were using x-ray and no radium. I have had the impression that most surgeons have not favored preoperative irradiation in operable breast tumors. I have not tried such treatment in early cases. In inoperable cases irradiation is the only treatment, and such treatment is especially indicated in inflammatory carcinoma of the breast, which should never be subjected to operative interference.

However, when surgeons of the training and experience of Drs. Bloodgood and Stewart advocate preoperative irradiation of early malignant breast tumors, we must consider what they say. X-ray and radium therapy have increased in efficiency. If I understand the reported cases rightly, irradiation caused all cancer cells to disappear, so why operate at all after such successful therapy, or would not thorough excision have cured these cases more surely than irradiation? There are many such surgically cured cases on record.

In definitely proven cancer cases the authors advise delay in operation for two or three months while the patient is being subjected to treatment by irradiation, but I doubt that most surgeons will be content to submit to such delay. Surely it is contrary to our teachings of the past. However, we are in the midst of new deals, and it may be that preoperative irradiation has come into its own. We must not close our eyes to progress. The mind is like a parachute: it functions when it is open. Certainly many of our results in the treatment of breast cancer are bad enough, even in early cases, and we should welcome new methods when they come from such authority.

Before closing, may I pay tribute to the senior author of this paper, Dr. Joseph Colt Bloodgood, a former Chairman of this Section, who died October 22, 1935, less than one month ago. One of Dr. Bloodgood's most important contributions to surgery was his great work on mammary carcinoma, not only in his teaching the profession, but in urging upon the public the necessity of seeking medical advice early when lumps appear in the breast. I remember a smaller, but still important, contribution which he made during the early days of cantonments in the World War, in calling attention to the inadvisability of operating upon varicocele, of

which there were thousands of cases among the soldiers. His strenuous protests were largely responsible for discontinuing the orgy of varicocele operations which had begun. I feel that we owe most to Dr. Bloodgood, however, for his efforts and example in making surgeons "pathology-conscious." He was his own pathologist, like John Hunter and Billroth, and as other surgeons should be. Few men of the present generation have given more to surgical pathology than Joseph Bloodgood, and his place will be hard to fill.

Dr. Stewart (closing).—Dr. Bloodgood arrived at the conclusions expressed in this paper only after a long study of the effect of irradiation upon malignant tumors. In tumors of the bone we have advised for years that irradiation be begun as soon as the presence of the tumor is known, while the history, x-ray plates and all examinations are being carefully studied for the most accurate diagnosis and efficient treatment. In many non-operative cases of carcinoma of the breast we have been unable to grow cancer cells after irradiation where before irradiation the cancer cells from the same patient gave us positive cultural growth.

Postoperative irradiation has not added to the five-year cures.

The lump in the breast may disappear under adequate irradiation to the tumor and the adjacent glandular areas, but we should not stop with this disappearance. The complete operation should be done after the local irritation from the treatment has subsided. We feel it is safe to delay this operation as long as three months without danger to the patient.

Early diagnosis as always gives the greatest number of cures. This should continue to be our goal: early diagnosis followed by adequate treatment.

Sufficient time has not elapsed to enable us to report five-year cures in cases of preoperative irradiation of operable carcinoma of the breast. We feel, however, that there is great possibility that preoperative irradiation will increase the number of five-year cures in carcinoma of the breast.

PLASTIC REPAIR OF FACIAL DEFECTS RESULTING FROM RADICAL EXTIRPATION OF CANCER*

By NEAL OWENS, M.D.
New Orleans, Louisiana

Plastic repair of facial defects following radical extirpation of cancer is modified by the resulting loss of tissue and the method of repair indicated is naturally determined by the extent and situation of the deformity. Defects which are minimal and which are in areas that permit approximation of borders without resulting distortion frequently may be closed satisfactorily by approximation of defect borders with interrupted sutures. A defect involving the complete loss of a part requires an extensive procedure, frequently one which involves the use of tubed pedicle skin transplants in combination with some suitable type of skin graft.

Satisfactory results frequently are obtained in the closure of defects by simple approximation of the borders of the defect. The closure in those cases is either by interrupted or intradermal sutures. In the former instance, closure is ordinarily stable and gives a satisfactory cosmetic result, whereas in the latter the repair is cosmetically better because the resulting scar is minimal. If there is tension when the defect borders are approximated by converging pressure from the fingers it is advisable to undercut the skin for a short distance about the borders of the defect. If the depth of the wound is more than superficial one suture may be taken advantageously in the subcutaneous tissues to lessen tension at the point of skin closure as well as to eliminate potential dead spaces.

Skin grafting is indicated in the repair of large surface defects where an approximation of the defect borders is impossible. In this type of defect the destruction is primarily in the skin, a factor which permits repair by skin grafting without subsequent depression deformity. There are three suitable types of skin graft which may be used on the face with satisfactory results: (1) the thin or Thiersch graft; (2) the intermediate or "split" graft; and (3) the full thickness or Wolfe graft. Skin grafts are transplanted portions of skin, varying in size and thickness, which are dependent for their blood supply upon areas on which they are grafted. True skin grafts do not contain more than the full thickness of skin. Thiersch grafts are cut as sheet-like portions of skin, including slightly more than the epidermis, and the area of the graft removed is frequently equal to 25 square inches. The Thiersch graft is indicated in the repair of surface defects which involve an area subjected to little trauma or pressure, where full thickness or intermediate grafts are not so essential. The intermediate or "split" graft has been popularized in this country by Blair[1] and Brown[2] in the repair of large surface defects resulting from burns. This graft is essentially the same as the graft referred to by Gillies as the "thick razor graft." The intermediate graft contains from one-half to two-thirds of the thickness of skin and is cut much the same as the Thiersch. Both grafts are cut by means of

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*Read in Section on Surgery, Southern Medical Association, Twenty-Ninth Annual Meeting, St. Louis, Missouri, November 19-22, 1935.

*From the Department of Surgery, Tulane University School of Medicine, Charity Hospital, and Eye, Ear, Nose and Throat Hospital, New Orleans, Louisiana.

A B

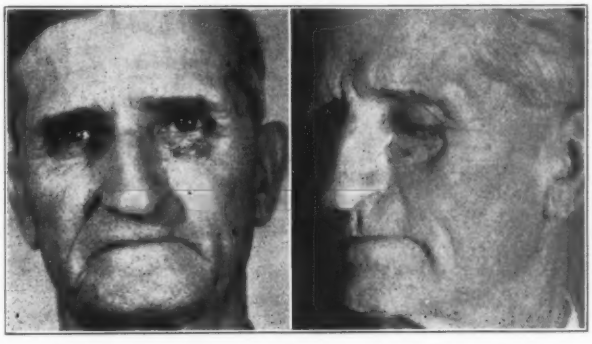
Fig. 1

(A) Photograph showing epithelioma over bridge of nose.
(B) Results following excision of growth and application of full thickness skin graft.

a long thin knife and are removed by passing the knife downward beneath the surface of the skin at the donor site after it has been drawn tense by means of small wood blocks which apply divergent pressure at their points of contact, or by means of the Blair suction box. By passing the knife downward, beneath the surface of the skin at the desired depth, with gentle back and forth sliding motion, the graft is removed to conform to the size and depth required. Successful removal of these grafts depends upon the constantly maintained skin pressure as well as the skill of the operator. Removal of these grafts is not easy and, as a rule, much time, patience, and practice are required. Following the removal of the grafts they are placed over the defect and are sutured to the entire border of the defect by No. 0000 silkworm gut sutures. Here and there the graft is sutured to the base of the defect by means of deep mattress sutures passing through the graft, into the floor of the defect and out again. Following the attachment of the graft by sutures a suitable pressure dressing is applied.

The full thickness of Wolfe[8] graft includes the entire thickness of skin with as little subcutaneous fat as possible. Subsequently this graft has a more normal appearance, is softer, and is more pliable than that obtained by other grafts. The full thickness graft should always be cut according to a pattern of the defect in order to insure normal skin tension when it is sutured into the defect, a factor which is most important in aiding the re-establishment of blood supply to the graft from the base of the defect upon which it is placed. The graft is held fixed to the borders of the defect by means of interrupted sutures of No. 0000 silkworm gut. Following the attachment of the graft to the defect border a suitable pressure dressing is applied.

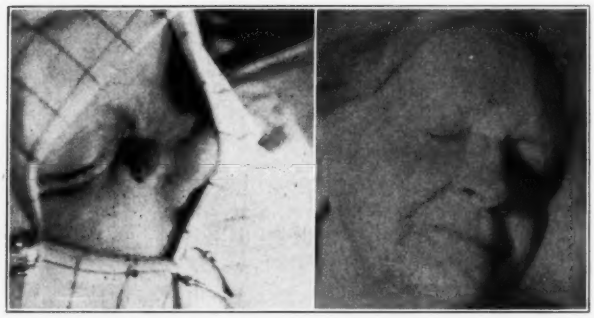
Defects which are larger and which show a destruction of subcutaneous fat as well as a portion of muscle are more satisfactorily repaired by means of a single pedicle skin transplant, since a repair by skin grafting would show a depression deformity which would have to be corrected later by an implant of fat graft. It is equally important to use this type of repair for defects situated in contaminated areas where varying degrees of infection are almost certain, since skin grafts do not tolerate infection nearly so well as the pedicle skin transplants. There are three types of single pedicle skin transplants commonly used:[3,4] (1) advancement; (2) rotation; and (3) sliding. Pedicle transplants differ from grafts in two respects: (1) they may carry varying amounts of subcutaneous tissue into the area to be repaired; and (2) they derive their blood supply through a remaining pedicle attachment which is not severed until complete anastomosis has been established between the defect and the skin pedicle. The principal difference between the three types of



A B

Fig. 2

(A) Photograph showing basal cell carcinoma involving entire left eyelid.
(B) Results obtained by excising entire lower lid followed by reconstruction with full thickness skin graft.



A B

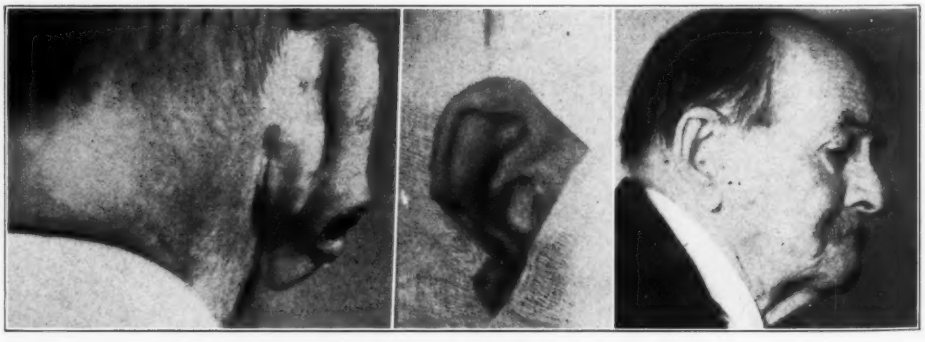
Fig. 3

(A) Epithelium involving skin at the inner canthus of right eye.
(B) Healed stage following repair by means of pedicle transplant from the forehead.

pedicle transplants is the manner in which they are shifted from their original site into the area to be repaired: an advancement transplant is one which is advanced upward or downward from its original site into the defect to be repaired without appreciably altering the plane of the pedicle surface; the rotation pedicle skin transplant is one which has to be rotated at its pedicle attachment in order to transfer it from its original site into the defect to be repaired and, as a result, varying amounts of torsion are applied to its pedicle; the sliding skin pedicle transplant is one which is shifted from its original bed directly forward into the defect, thus placing tension upon the skin transplant in a line which is directly away from the pedicle. Pedicles are fashioned according to a pattern of the defect to be repaired. One of the most satisfactory methods for fashioning these flaps is described by Sir Harold Gillies[5] as follows:

"The idea is to imagine the operation completed and the flap transplanted to its new home. Now plan to get that piece of skin back to a suitable donor site by reversed stages. It will be found to take up quite unexpected positions there, but the comforting thought arises that, when cut to pattern in this ascertained position, and the flap raised, it will fit the area to be grafted precisely and without tension."

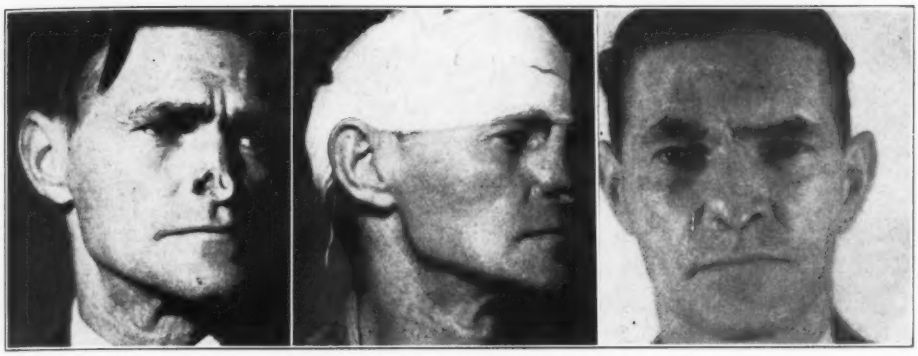
Defects requiring massive restoration of tissue for correction are best repaired by means of a double pedicle skin transplant, since it requires that skin be transferred from a distant site. This type of transplant was devised by Sir Harold Gillies[6 7] while reconstructing some of the massive defects resulting from war wounds at Sidcup, England. Many of the defects encountered in these cases were so massive that it was necessary to transplant unusually large areas of skin for their reconstruction, thus necessitating their removal from distant donor sites. The hazards of such distant transfer of massive skin flaps were so great that untoward results were feared. Adequate blood supply was the factor which gave greatest concern, but infection, shrinkage and associated fibrosis, due to the massive exposure of the uncovered subdermal portion of the flap, were factors which caused considerable worry. In attempting to obviate these troublesome complications the



A B C

Fig. 4

(A) Photograph of epithelioma involving the helix of right ear.
(B) Defect resulting from excision of epithelioma.
(C) Result obtained from repair by means of single pedicle skin flap rotated from the mastoid region.



A B C

Fig. 5

(A) Defect of nose following removal of cancer by means of radium and cancer salve.
(B) Intermediate stage following reconstruction by means of forehead pedicle flap.
(C) Photograph showing final result.

presently used technic for the formation of the tubed pedicle skin flaps was devised. The double pedicle skin flaps are attached at each end by means of a connecting pedicle and are fashioned into a closed tube by approximating the two longitudinal borders of the flap in such manner that skin entirely surrounds the outer surface of the tube. The parallel borders of the tubed pedicle skin flap, which have been approximated by folding, are closed by means of fine interrupted sutures, thus completing the formation of the tube. The defect beneath the tubed pedicle thus formed is closed by simple approximation of the borders of the defect by means of interrupted sutures of silkworm gut. By means of the tubed pedicle skin flaps large areas of skin can be brought to a defect from a remote portion of the body without altering the skin or subcutaneous tissues, and when the tube is opened, after being carried to the recipient area by means of some movable member, the texture of the skin is pliable and the subcutaneous fat contains little or no scar. In repairing large defects by means of a tubed pedicle flap, the tube is formed and permitted to remain undisturbed for a period of two to three weeks, after which time one pedicle is severed and anastomosed to some movable member, as the arm or leg. Following a second similar period of waiting, the other pedicle is detached and carried to the defect to be repaired, where it is sutured into position. The movable member affords blood supply to the tubed pedicle after it is brought into the defect to be repaired until a blood supply can be established between the site of the defect and the pedicle, after which time the pedicle is severed at its point of anastomosis with the arm or leg and the remaining detached portion is sutured into the unrepaired portion of the defect.

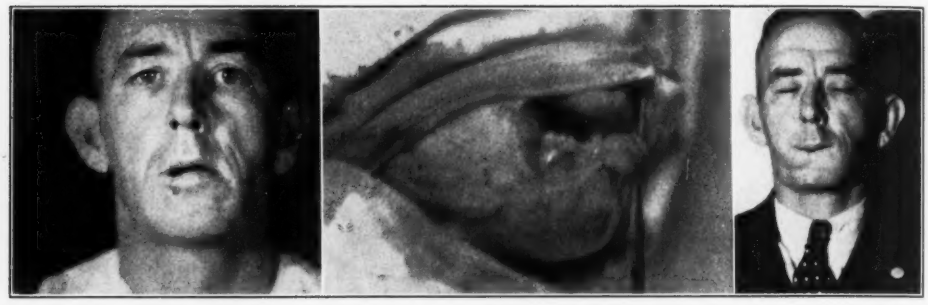
In cases with advanced cancer the defects following extirpation are frequently so extensive that repair by means of tubed pedicle skin flaps alone is not feasible. Many of these cases require the use of the tubed pedicle flap in combination with the single pedicle flaps and frequently skin, fat, and cartilage grafts have to be included. Where these procedures are necessary, in combination, the methods are identical with those described above.

Defects resulting from the extirpation of pre-

A B

Fig. 6

(A) Defect of the nose following extirpation of basal cell carcinoma.
(B) Final result.



A B C

Fig. 7

(A) Photograph showing squamous cell epithelioma of the lower lip. Note the contracture at the right angle of the mouth which resulted from the application of radium.
(B) Photograph showing defects resulting from excision.
(C) Result following repair by advancement pedicle flaps. A slight secondary adjustment will afford good cosmetic results.

cancerous growths or early localized cancers are commonly small enough to permit satisfactory closure by means of simple approximation of the defect borders with interrupted or subcuticular sutures. If cosmetic results are particularly important, the closure should be made by a subcuticular suture rather than by interrupted ones, since the former gives a minimal amount of scar.

Defects which are sufficiently large to make it injudicious to attempt closure by means of direct approximation of the defect borders should be repaired by means of some suitable type of skin graft. Defects over the forehead are satisfactorily repaired by means of a Thiersch graft, and frequently small defects over the nasal bridge are satisfactorily closed by this type of reconstruction. The majority of facial defects are most satisfactorily repaired by means of intermediate or full thickness grafts. Defects healed by means of the intermediate or full thickness grafts show considerably more stability and less tendency to contract, this latter factor being quite important when the defect is near the eyelid or angle of the mouth because of the possibility of ectropia or distortion to the mouth. Probably the ideal graft for the reconstruction of a lower lid is the full thickness, and, since it is cut identical in size and shape with the pattern of the defect and with its minimal tendency toward contraction, should produce no subsequent ectropion. The ideal skin for an eyelid repair is that from either the forehead or the mastoid region, since the skin in these two areas more closely simulates the color and texture of the skin of the face than any other available portion.

Defects which show a depth greater than skin thickness are repaired with better cosmetic results by a single pedicle skin transplant, since fat can be carried into the defect with the skin flaps, thereby filling in the depression. If this type of repair is attempted by means of a skin graft there is invariably a depression deformity which results and it is frequently necessary to fill out the contours at a subsequent date by means of a fat graft. Defects about the inner canthus of the eye are best repaired by means of some type of pedicle flap, because (1) they are constantly subjected to contamination and subsequent infection, which is commonly not sufficient to destroy a pedicle flap, but which is not tolerated by skin grafts; (2) they are crater-like and, therefore, inaccessible for the maintenance of adequate pressure, a factor also essential to the success of a skin graft; and (3) these defects are predominantly avascular due to their proximity to the periosteum, and consequently the establishment of circulation with a graft is hazardous. Defects of the ear resulting from extirpation of cancer growths are satisfactorily repaired by means of single pedicle skin flaps outlined and raised from the mastoid region. A pattern of the defect is taken, identical in size and shape with that of the defect, and an area identical with the pattern is outlined over the mastoid region. The portion of the pattern which represents the pedicle is then held firmly fixed to the mastoid skin and the remaining portion of the pattern is raised and carried into the defect in such way that the pedicle flaps when dissected up can be brought into the defect without tension. It is essential that the size be ample to fill the defect, thereby pre-

serving the normal skin tension after it is sutured into place. If the above trial proves that the area outlined is correct it is then dissected free from its underlying subcutaneous tissues and brought up into the defect where it is approximated to the upper and lateral borders of the defect by means of fine interrupted sutures. At the end of the usual two-week period which is permitted to pass before the pedicle is severed, the posterior surface of the pedicle, which was originally bare of any epithelium, is, as a rule, completely epithelialized. The final stage consists of severing the pedicle and anastomosing its distal border to the lower border of the ear defect. The slight defect resulting from its complete separation from the mastoid skin is closed by means of interrupted sutures. The original defect over the mastoid, caused by raising the pedicle flap, is usually closed by direct approximation of the borders with interrupted sutures.

Radical extirpation of cancer in the advanced stages commonly results in massive defects and the repair of these varies with the amount of destruction produced. The defects in this group of cases vary from a moderate loss of skin with underlying fat and muscle to the more massive types of destruction which entail the complete loss of a part. The majority of these defects are too extensive for repair by means of skin grafting. Reconstruction by means of some type of single or tubed pedicle flaps in association with some form of grafting, even including fat and cartilage, is usually indicated.

Defects resulting in a complete or total loss of the nose require a total rhinoplasty. This procedure generally entails the use of a forehead flap together with lateral inversion flaps and some type of skin grafting. Reconstruction of the nose to obtain satisfactory and permanent results has two minimal requirements: (1) the reconstruction of the nasal lining; (2) the reconstruction of the outer nasal covering. In those cases in which there has also been a loss of bony or cartilaginous structures, it is necessary to supply this deficit by means of a cartilaginous implant. Gillies demonstrated in a series of cases the expediency of complete reconstruction of the nasal lining, in that a reconstruction which in its early postoperative stage was entirely satisfactory would months later shrink into a distorted nose which had no resemblance to its original contour. An analysis of this unpleasant regression revealed a very obvious basic fact: the nose which had been so satisfactory in its early reconstruction stage had been considered entirely from the point of external appearance, but no consideration had been given to the condition of the underside of this otherwise satisfactory covering, or to the associated pathological changes which would subsequently follow. An analysis of the problem revealed that the underside of the skin covering the newly formed nose was entirely denuded and that before areas as extensive as these could epithelialize, the usual concomitant inflammatory changes invariably took place. The following changes were found: chronic granula-

A B C

Fig. 8

(A) Photograph showing extensive involvement of entire lower lip from squamous cell carcinoma.
(B) Photograph showing in detail the extent of involvement.
(C) Result following repair by sliding pedicle flap. Note small area of necrosis in center of reconstructed lip due to extreme tension under which closure was made. This subsequently closed satisfactorily.

tions, over-production of scar, and subsequent contractions. From the above analysis it was felt that a restoration of the nasal lining, simultaneous with the restoration of the nasal roof, was essential. Cases repaired according to this technic proved the wisdom of the analysis and as a result we are now able to perform a rhinoplasty with the assurance that our chances of success are good. In the reconstruction of a nose a pattern of the defect is taken to enable the operator to fashion lateral pedicle flaps which are inverted to form the nasal lining. If the defect involves one side of the nose the flap is usually outlined from the skin of the opposite side. However, if the defect is more extensive and involves both sides of the nose the pattern is usually bisected and the resulting two patterns are folded outward to approximate with the skin of the nose or cheek on their adjacent sides. Following the outline according to pattern, the flaps are then dissected up, leaving the pedicle attachment adjacent to the nasal defect so that the skin surface falls to the inside of the nasal cavity when inverted. If the defect is on only one side of the nose or a portion of one side, the flap is inverted and anastomosed to the border of the defect by means of interrupted subdermal sutures placed in a manner which does not permit them to penetrate into the nasal cavity; if the defect is on both sides of the nose, the lateral flaps are turned toward the midline with their skin surfaces toward the inside of the nose, where their free borders approximate and are anastomosed with each other as well as to the remaining border of the defect. The above procedure completes the reconstruction of the nasal lining, but concomitantly increases the defect in the skin covering the nose. A pattern of the latter defect is taken and an area of skin to conform to the size and shape of the pattern is next outlined over the forehead in a position which will permit the pedicle attachment to incorporate the skin just above and slightly medial to the eyebrow on the side of the defect. The pedicle flap is then raised and rotated downward on its pedicle to be sutured to the border of the external defect. The pedicle is permitted to remain undisturbed for a period of two weeks before it is severed. After this period it is severed and the remnant of the pedicle is carried back to its original bed, where it is reincorporated into the skin covering the forehead. The forehead defect following the formation of a pedicle flap of this type is commonly so great that repair by means of a skin graft is indicated and to facilitate prompt healing a split graft is usually applied. At the end of the two-week interval when the pedicle is severed it is frequently found that the forehead defect has entirely healed, and it is necessary to remove a portion of viable skin graft in order to permit the rein-

A—top left. B—top right.
C—bottom left. D—bottom right.

Fig. 9

(A) Photograph showing extensive destruction following application of radium for treatment of basal cell carcinoma. Note the destruction of the lower eyelid, the skin over the greater part of the right side of face, and the destruction of the bony roof of the antrum.

(B) Single pedicle forehead flap brought down and attached around the border of the antral defect to reconstruct the antral lining. Skin surface is inverted in such manner that it will lie within cavity of the antrum.

(C) Photograph showing a tubed pedicle skin flap transplanted from the abdomen to repair defect resulting from excision of involved skin over right side of face.

(D) Final result following restoration of the antral cavity, the greater surface of the right side of the face, and the lower eyelid.

sertion of the remnant of the pedicle flap back into its original bed. In those cases in which there has been loss of bony or cartilaginous framework it is necessary to restore the nasal bridge by means of a cartilage implant, and where time and the patient's condition permits, this implant is buried beneath the forehead skin in proper position to be carried downward, in position, as an incorporated part of the pedicle flap. In order accurately to implant the cartilage, an area of skin is outlined in precisely the same manner as described above and a shallow incision is made around the entire circumference of the outline, in order that a slight scar may remain to guide in the ultimate removal of the pedicle flap. The cartilage, which has been removed from the fused portion of the seventh and eighth costal cartilages, is next shaped to conform to estimated measurements and inserted beneath the skin outlined for the pedicle flap. Following a period of weeks the cartilage becomes sufficiently incorporated to enable the operator to raise the cartilage and swing it down as an integral part of the pedicle flap. It is frequently necessary, after the reconstruction of the nose is complete, to make some minor adjustments, here and there, in order to produce the desired cosmetic results.

Extirpation of moderately advanced cancer of the lower lip frequently results in the removal of all or the greater part of the lip and requires the reconstruction of an entire lip to render a satisfactory functional result. The advancement single pedicle flap affords the most desirable type of reconstruction because it carries sufficient substance into the newly formed lip to obviate tightness and distortion. Lips reconstructed by this method usually have a normal fullness and as a result the patient is not concerned with a distortion which frequently results from other methods of repair. Repair may be accomplished with a fair degree of ease by sliding flaps taken from the central portion of the cheek, but considerable tension is required to draw these anteriorly and a tightness usually results which not only distorts the mouth but causes difficulty in eating and talking. Repair by means of advancement flaps is decidedly the method of choice. The reconstruction of a lower lip by advancement single pedicle flaps entails the consideration of two separate sets of flaps: (1) the skin flaps; (2) the mucous membrane flaps. The first stage in the reparative process is the formation of a pattern of the defect. The pattern is then bisected in order to facilitate the formation of flaps of equal size from either side of the defect. The lateral border of each pattern is held firmly approximated with the skin forming the lateral border of the defect and the medial border is swung downward and outward until the entire pattern lies over normal skin. The pattern is next swung back up into its original position to insure that the lateral border has not shifted and that the length of the pedicle will be ample. After repeating the shifts a sufficient number of times to feel sure that the proposed outlined area is correct, a pedicle of skin identical in size and shape with that of the pattern is outlined and dissected up, carrying a thickness of skin and muscle sufficient to give ample substance to the lip. The same procedure is carried out on the opposite side and after completion, if the pedicles have been cut properly, they will advance upward into the defect without difficulty and their medial borders will approximate without tension. The formation of mucous membrane flaps is the next consideration, for these must be dissected up and advanced into a forward position in order to restore the buccal sulcus, a covering for the denuded posterior surface of the pedicle skin flaps and a satisfactory vermilion border. The technic for outlining the mucous membrane pedicle flaps is identical with that described for the skin pedicle with the exception that it is considerably more difficult to make accurate measurements within the mouth, and for this reason there is greater possibility of error. Following the dissection of the mucous membrane flaps they are advanced into the defect and their lower borders are sutured to the lower oral border of the defect. If measurements have been correctly taken their medial borders will approximate without difficulty. These are held in apposition by interrupted sutures of black silk. The intra-oral defects resulting from the advancement of the mucous membrane flaps as a rule can be closed with little difficulty by direct approximation of the borders with black silk. After the approximation of the mucous membrane flaps, the skin pedicles are advanced upward into the defect and held in apposition by means of interrupted sutures taken through their medial borders. The mucous membrane flaps are then drawn over the upper surfaces of their respective skin pedicles and the upper border of each mucous membrane flap is sutured to the upper outer border of its respective skin pedicle. The lower borders of the skin pedicle are attached to the lower skin borders of the defect by means of inter-

rupted sutures of black silk and the borders of the lateral defects, resulting from the formation of the skin pedicle, are closed by direct approximation where possible. It is necessary at times to make minor adjustments in order to facilitate a closure of these lateral defects, but as a rule this repair causes little difficulty. Following the complete reconstruction of the lower lip a stab wound is made through the uninvolved skin beneath the mental process and through this a rubber tissue drain is inserted and carried upward to a position which will facilitate adequate drainage. The insertion of the rubber drain is of considerable importance and probably is a prominent factor in obtaining healing by primary intention. Frequently a small area of central necrosis is experienced at the upper point of anastomosis between the two skin pedicles along with varying amounts of necrosis of the upper border of the mucous membrane flaps. This complication is rather to be expected and causes no untoward ultimate result, since there is ample substance incorporated into the newly formed lip to permit a secondary adjustment when healing has occurred.

Major defects are occasionally seen which involve the loss of a large portion of the skin over one side of the face, including the loss of an entire lower eyelid and the bony roof of the antrum. A defect of this type presents the complex problem of restoring the antrum, reconstructing the lower eyelid, restoration of the skin covering the greater surface of one side of the face, and eventual restoration of the normal facial contour. Satisfactory reconstruction of an antral defect requires a reconstruction of the antral cavity and since the bony roof of the antrum has been destroyed, this can only be done by means of a hairless skin transplant. The anastomosis of a hairless skin transplant with the borders of an antral defect can best be accomplished by means of a single pedicle forehead flap, raised on a temporal pedicle to insure adequate blood supply, which is rotated downward and sutured into the border of the defect with the skin surface inside the antral cavity. After a period of two weeks the pedicle attachment at the antrum is severed and the border of the pedicle at the site of the detachment is then anastomosed with the remaining portion of the antral defect. The unused portion of the temporal pedicle skin flap is carried back and sutured into its original bed. The forehead defect produced by the formation of the temporal pedicle flap is best repaired immediately following the formation of the pedicle by means of an intermediate skin graft. A facial defect of the above mentioned proportions requires considerably more skin for repair than is available on the face, thereby necessitating its transplantation from some distant part. The abdomen normally offers the best reserve for removal of large quantities of skin and produces a type which satisfies all normal requirements. Transfer of a large quantity of skin from the abdomen to the face can be accomplished satisfactorily only by means of a tubed pedicle skin transplant. A pattern of the facial defect is made and an area identical in size and shape is outlined on the abdomen. The area of skin outlined is dissected free from its underlying subcutaneous tissue and fashioned into a tubed pedicle transplant with its pedicle attachments undisturbed. After a period of two weeks one pedicle is severed and anastomosed to the dorsum of the hand selected as the movable member to carry the transplant to the face. A similar period is allowed for establishment of circulation between the hand and the pedicle when the second pedicle is detached from the abdomen and carried to the face by means of the arm. An anastomosis is established between the last severed pedicle and the face and circulation is permitted to establish itself for a period of two weeks before the first pedicle is detached from the hand. At this stage one-half of the tubed pedicle has been opened and attached to the upper borders of the facial defect where it has remained for two weeks. The second half, which is detached from the hand at the end of the third two-week period, is at this time opened and attached to the uncovered portion of the facial defect to complete the repair. At this last stage it may be obvious that the facial contour will not be normal without the implantation of a fat graft. If a fat graft is necessary, it is best removed from the abdomen and inserted beneath the skin pedicle before final closure is complete. The restoration is complete at this stage except for the reconstruction of the lower eyelid. This is best accomplished by means of a descending forehead pedicle, swung down to form the outer surface of the lower lid. The inner lining and conjunctival sac are usually formed by dissecting up a remnant of conjunctiva which is commonly adherent to the upper border of the skin transplant which had been brought up from the abdomen.

CONCLUSIONS

(1) Facial defects following the radical ex-

tirpation of cancer are modified by the resulting loss of tissue and the method of repair indicated is, therefore, determined by the extent and location of the deformity.

(2) As a result of observation of complications resulting from certain types of treatment, the following suggestions are made: (1) growths involving skin over cartilage should not be subjected to radiation because of the high percentage of cartilaginous destruction which follows this procedure; (2) treatment of cancer by x-ray or radium should always be by a specialist, competent through long experience, to apply radiation in amounts which are adequate. Patients are too frequently seen who have received inadequate radiation and as a result they subsequently seek treatment for lesions, because of late manifestations, which are hopelessly advanced; (3) microscopic study of all tissue removed, by means of the frozen section method, should be routine. By means of this technic more involved tissue will frequently be removed which otherwise would have been permitted to remain because of its normal macroscopic appearance.

(3) Much can be accomplished in the restoration of defects resulting from the eradication of cancer. Many patients would be less skeptical in subjecting themselves to the eradication of a growth if they could be assured that unsightly deformities would not be a necessary sequel.

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DISCUSSION (*Abstract*)

Dr. Vilray P. Blair, St. Louis, Mo.—This paper has a tremendously important basic significance in that it calls attention to the fact that the deformities and losses that may be an unavoidable incident to efficient treatment of cancer of the face can be corrected both regarding function and appearance. It is more than probable that the fear of such deformities is one of the reasons why cancer of the mouth and face does not, on the average, receive as good treatment as in other parts of the body, especially exposed surfaces. In the short time allotted Dr. Owens has presented a tremendous amount of information, but it was not sufficient for much more than the high spots. I know that if time had permitted he would have still further emphasized the necessity of making a sharp distinction between the treatment of the cancer and the repair of the defect; for, as in cancer of the breast or any other part where a destructive obliteration is indicated, this latter should be done without thought of how the repair is to be made. One can always count on having sufficient material to make a repair, and more detailed calculations had best be postponed until the control of the cancer has been assured, or at least can be reasonably inferred.

Following excision of a malignant growth, the time at which the repair should be made is always a matter of special interest. Where the growth occupies only a small area it is possible, in many instances, to remove sufficient tissue to give reasonable assurance of control and at the same time make an immediate repair from neighboring or transplanted tissues, but in the more extensive growths, it is usually better to get rid of the growth before risking the wastage of repair material that would be difficult to replace. On the other hand, cancer of the face and mouth occur in many people at a very useful time of life, and in many instances one can give them one, two or more years of life free from recurrence in which to continue their activities, even though it may not result in a five-year cure. However, in the majority of cases, the repair must be made before ordinary gainful occupation can be resumed. We have selected three months as about the period we allow to elapse before we begin the actual repair, though in the more promising cases we often prepare the flaps in the meantime. Three months will give time for exfoliation of bone of the lower jaw which has been devitalized by the cautery, and also permits scarring completely or incompletely of the soft tissues after destruction with diathermy, actual cautery or escharotics.

Dr. Earl C. Padgett, Kansas City, Mo.—The fundamental principles for the repair of soft tissue facial defects have been very well reviewed by Dr. Owens. Dr. Blair covered some of the philosophy applicable to cancer and the repair of its ravages in this region. No one does it better. If one might be pardoned for a slight shift to the left, so to speak, I should like to continue with some of the philosophy of treatment as it has impressed me.

I was brought up in close contact with what I consider the very best surgery of the older radical school. At present in certain circles I think there is a distinct tendency to belittle the results obtained by this older type of approach to the problem. On the contrary, the routine use of radical surgery without regard to the pathological principles involved or the results irradiation has shown, is now passe, I believe.

Undoubtedly radium and intense x-ray therapy have caused a transition in the therapy of cancer in this region. About a dozen years ago it began to be quite evident to those caring for cancer about the face, mouth and jaw, that besides being familiar with and able to do radical surgery, one has to be familiar with and able to use the principles of irradiation. But now, it seems to me that the enthusiasm for a type of therapy entailing very little surgery has been overdone in certain enthusiastic circles.

The newer methods have, however, thrown the older method on the defensive which I think has been of

value to the surgery of this region. Thereby surgery has been forced to undergo a refinement and possibly a limitation. As to the refinement, the endothermic knife has helped by allowing a more bloodless destruction or excision which tends toward preciseness of excision or destruction. The lessened loss of blood tends to lower mortality. In this region no longer can a surgeon argue that because uncured cancer has 100 per cent ultimate mortality, a rather high mortality is allowable unless the situation is such that irradiation offers little or no chance. The older routine operations of removing a certain organ, as, for instance, one-half of the tongue, largely have been supplanted by removal only of the tissue which the pathological necessities of the case dictate. By this I would not have you think that radical removal is never necessary. For instance, in a case where a lymph node involved with metastatic adult squamous carcinoma has become attached to the mandible in the submaxillary or submental region I think radical excision with a lengthwise removal of one-half or even a sectional removal of the jaw along with the cancerous tissue is good surgery because irradiation offers practically nothing to such a lesion and surgery has held up recurrence for a number of years and even cured 4 to 5 per cent of such cases. I do not entirely subscribe to the dictum that when carcinoma has broken through the capsule of a lymph node, surgery is contraindicated. The carotid artery is about all that one cannot remove justifiably in certain rare instances.

Certainly one familiar with the principles and results of irradiation will be well aware that for certain local lesions where a lethal dosage can be applied, irradiation is simpler and the less mutilating procedure and seldom entails much risk to life. Surgery has lost its appeal in such situations. On the other hand, heavy irradiation is most often not a comfortable procedure. Sometimes I have thought that if I were given the choice of surgery and heavy irradiation for myself with curative factors the same, that surgery would be selected as being the most comfortable. I say this to point out that in some instances surgery has been maligned unjustly. Irradiation striking towards a lethal dosage for the tumor is no joke for the patient.

When a lethal dosage of irradiation cannot be given, as for instance to the lymph nodes involved, or even possibly involved by adult squamous cell carcinoma, I think irradiation enthusiasts have overstepped the bounds of sound reasoning when they still advocate a policy of sublethal dosage and procrastination.

The advances made in our knowledge of relative radiosensitivity have shown that certain radiosensitive tumors can be selected in which surgery is of no great value and that the application of correct irradiation principles gives quite striking results.

There is also a middle group of lesions in which the application of the principle of both irradiation and surgery will, I believe, ultimately be considered the method most likely to result in a cure.

Finally, to illustrate a present day trend, I show several lip cases operated upon from five to eight years ago cured for five years or more by excision followed by various types of plastic procedures. In some of these now the same results can be shown so far as the local lesion is concerned by the proper use of radium without having to resort to plastic surgery. The results are good, but in some of them excision is not now necessary. A similar situation was present when six years ago I removed a carcinoma of the cheek and then built in the cheek with a skin flap. On the other hand, I have several noses and also a few lips originally involved with carcinoma which were healed with radium, but in which the destruction by the combination of the tumor and the irradiation necessitated a plastic repair to give a good result.

The problem then today is to learn how to select and correctly apply therapy in each individual case without bias according to principles already known. One must therefore know the pathological principles involved, know what surgery has to offer and finally know what a combination of surgery and irradiation will do.

At present, when one works along these lines more can be offered than ever before, not only of palliation but also of increased chance of total disappearance, to the individual patient suffering from malignant disease about the face, mouth and jaws.

Dr. Owens (closing).—It was intended to limit this paper to a discussion of repair of defects resulting from radical extirpation of cancer of the face, since time would not permit a discussion of methods of treatment. Under no circumstance do we minimize the extreme importance of proper procedures in the extirpation of cancer. On the contrary, we feel that the point of major importance is that of proper eradication, for here hangs the balance which determines whether the patient has been benefited and subsequently whether a life has been saved. Dr. Blair well summarized our attitude in regard to treatment when he stated that treatment of cancer in cases in which destructive obliteration is indicated should be done with no thought of subsequent repair. To insure proper treatment each case is considered in two phases: eradication and repair. When considering the treatment of cancer the sole thought is eradication and cure. Following this, when a safe period has passed and no recurrence has been noted, the second phase is considered, and repair is attempted. In following the above routine we feel that cancer is best treated, since eradication is not tempered by thoughts of repair.

The treatment suggested by Dr. Padgett is essentially that which we advocate and follow. I believe that we are inclined to bear more to the right than he suggests, however, since we radically extirpate all tumor tissue with ample margin, frequently with the aid of plumber's cautery, and follow this procedure with a radical dissection of the glands of the neck. Where indicated, irradiation is given in conjunction with this procedure.

We feel that thorough extirpation should always be carried out with the aid of biopsy done by the frozen section technic, for in this manner borders and wound depth are clearly outlined, and the operator knows within four to five minutes whether all cancer tissue has been removed. The frozen section biopsy has shown, in many cases in which we felt ample margin had been given in removing tumors that, even though there was no macroscopic evidence of tumor tissue present, definite and considerable cancer tissue had been left behind. The frozen section biopsy is of inestimable value in this last mentioned group, because many of these can be cured when treated properly at the first operation. If handled improperly, they may be denied a permanent cure and frequently early metastasis is found.

TUMORS OF THE THYROID GLAND*

By WM. F. LAKE, M.D.
and
A. J. AYERS, M.D.
Atlanta, Georgia

Tumors of the thyroid gland have not been studied by the average pathologist so thoroughly as tumors involving other organs of the body. Also it is generally known that there are some pathological changes in this gland that are similar to changes seen in other organs, but are more difficult to diagnose. In 1921, Wilson reviewed the literature on thyroid tumors and in reporting his experience at the Mayo Clinic, said:

"Correct early diagnosis of malignant tumors of the thyroid is made probably less frequently than of malignant tumors involving any other organ of the body."

The work of Wilson, Graham, Pemberton, Lahey and others has given to the profession valuable information concerning the various diseases involving the thyroid gland. Thyroid pathology, as seen by the clinical pathologist of today in the general hospital or the private laboratory, has been steadily increasing in volume during the past decade. Many important studies on the tissue changes of this gland have been worked out by the surgical pathologist and the tissue pathologist and if each will make good the opportunity to study the many thyroid diseases, there will be a still greater increase in the next decade.

The histological examination of any tumor is a most important study for the surgeon and often of inestimable value to the patient. We as pathologists should endeavor to show the profession that a microscopic examination is very necessary and should be made on many surgical tissues that are removed and sent to us for gross examination. The pathologist and the surgeon do not always recognize the nature of a neoplastic growth when seen in the gross state and if no microscopic examination is made, the proper diagnosis will not be made. There are many difficult problems of the thyroid gland that will be solved or better understood when the profession knows more about the gross and microscopic pathology of the gland.

During the past year at the Georgia Baptist Hospital, we have studied sixty thyroid specimens removed at operation. There were four malignancies in the group; 6.6 per cent of the series showed a well developed carcinoma. Two patients of the malignant group died soon after the operation and we were unable to secure an autopsy in either case. As this study continues from year to year there will probably be a drop in this high percentage of malignancies. There were three other very interesting thyroids in this series of sixty cases, one of which has been reported and published by Drs. D. Henry Poer, T. C. Davison, and E. L. Bishop. From the group, we are reporting in detail two cases of chronic thyroiditis, Riedel's type, one case of struma lymphomatosa (Hashimoto) and two cases of advanced carcinomas of the thyroid gland.

CHRONIC THYROIDITIS

(RIEDEL'S AND HASHIMOTO TYPES)

A large number of descriptive terms are used by the authors of recent literature dealing with this unusual and interesting disease of the thyroid gland. Among them are: chronic thyroiditis, chronic productive thyroiditis, ligneous thyroiditis, woody thyroiditis, struma lymphomatosa, Riedel's struma, benign granuloma, and granulomatous thyroiditis.

Riedel, in 1897, was the first to make a report of an unrecognized condition of the thyroid which was characterized by enlargement, firmness, and extensive adhesions outside the gland. Clinically the condition looked malignant but the histo-pathological study of the tissue showed a marked round cell infiltration, extensive fibrosis throughout the gland and an unusual change in the follicles with a reduction of the colloid. Riedel regarded the findings as the results of an inflammatory process. In 1912, Hashimoto reported the data in four cases which he had studied. The clinical findings were much the same as those reported as Riedel's struma but the histo-pathological examination showed in addition to the round cell infiltration, the formation of lymphoid follicles and many germinal centers. This had not been observed before and he reported the condition as struma lymphomatosa. In 1922, Ewing made a very careful study of a number of cases that fit the description of struma lymphomatosa, and it was his opinion that Hashimoto struma was not an entity but was an early stage of Riedel's struma. Ewing's views received general acceptance for a number of years and perhaps his views are more widely accepted today than

*Read in Section on Pathology, Southern Medical Association, Twenty-Ninth Annual Meeting, St. Louis, Missouri, November 19-22, 1935.

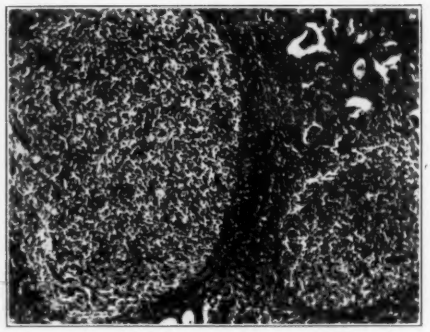

Fig. 1
Case 1. Low power. Struma lymphomatosa (Hashimoto).

those of any other author. In 1931, Graham reviewed the cases in the literature and included four cases of his own in a paper on the same disease of the thyroid. He contends that struma lymphomatosa and Riedel's struma are separate disease entities and that Riedel's struma is not preceded by struma lymphomatosa.

We have had the opportunity within the past year to study the clinical and microscopic findings of a number of pathological conditions involving the thyroid gland. In this series there are two cases of thyroiditis of the Riedel's struma type and one case of struma lymphomatosa (Hashimoto type). The criteria for the diagnosis of these unusual pathological conditions were the clinical findings, the physical signs at the time of operation and the histo-pathological examinations made of several thyroid tissues. To make the cases complete we have tried to observe all the data suggested by Graham, for the purpose of orienting ourselves in regard to this problem.

Case 1 (13,144).—Mrs. J. L. C., a white housewife, aged 35, gave a family history negative for goiter. Her chief complaints were an enlarged thyroid and nervous indigestion. The onset occurred four years previously, when she first noticed that she was nervous. For the previous two months she had noticed an enlargement of the thyroid gland, more pronounced on the right side. There was some tightness in the throat at times, but no difficult breathing. Her pulse was 86, blood pressure 120/86 and the basal metabolism test was minus 3 per cent. The Wassermann and Kahn tests were negative.

Pathological examination: A small mass of thyroid tissue, 3 x 10 cm., slightly nodular and of greyish pink color. The capsule was slightly thickened. On section, the tissue was firmer and more friable than is the normal thyroid structure. There were no calcified areas, no cysts, no adenomas and no abscessed areas in the gland.

On microscopic examination the sections showed a very small amount of colloidal material and the few remaining vesicles were small and atrophic. There was a marked round cell infiltration with many lymph follicles and germinal centers and some fibrous tissue throughout the gland. There was no normal thyroid tissue and most of the epithelial structure of the gland had been destroyed. The whole picture was very much like lymphoid tissue (*Figs. 1* and *2*). The diagnosis. Struma lymphomatosa of the Hashimoto type.

Case 2 (13,435).—Mrs. J. W. R., aged 53, a white woman, occupation, matron, reported that both grandmothers had had goiter. Her chief complaint was of an enlarged thyroid gland, pain in the neck and behind the ears. There was no loss of weight. In 1918, she noticed a small lump in the neck which had gradually increased in size and at present there was a large nodular mass measuring 12x10 cm., not tender and with no areas of fluctuation. The thyroid was firmly fixed to the trachea and surrounding tissues, indicating fibrosis outside the thyroid gland. There were no toxic symptoms. Her pulse was 86, blood pressure 126/70. The basal metabolism test was not recorded. Wassermann and Kahn tests were negative.

Pathological examination: Two large masses of thyroid tissue partially covered with a fibrous capsule, measuring 10 x 5 cm. and 9 x 5 cm., weight 85 grams. The tissue was very firm and nodular. On section it had a peculiar greyish brown color and showed marked fibrosis throughout the gland. There were no cysts, no abscesses and no areas of calcification.

On microscopic examination, all sections showed a small amount of colloidal material with a marked increase in fibrous tissue and a moderate lymphocytic infiltration. There were a few lymph follicles and a few germinal centers. All sections showed a destruction of the epithelial structure and there was no evidence of tuberculous or malignant changes (*Figs. 3* and *4*).

The diagnosis. Chronic thyroiditis of the Riedel struma type.

Case 3 (13,625).—Mrs. T. H., a white woman, aged 49, reported no history of goiter in the family. Her chief complaint was an enlarged thyroid gland and nervousness. The onset occurred seven or eight years previously, when she had noticed an enlargement of the

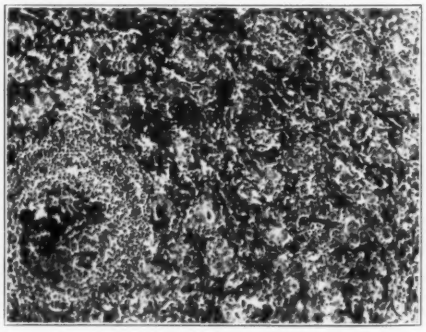

Fig. 2
Case 1. High power. Struma lymphomatoso (Hashimoto).

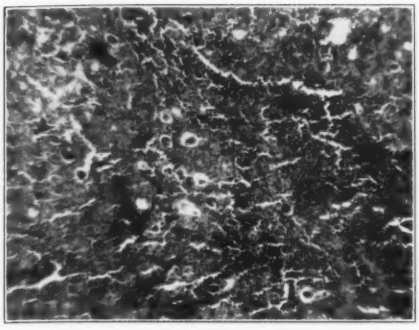

Fig. 3
Case 2. Low power. Chronic thyroiditis (Riedel's struma type).

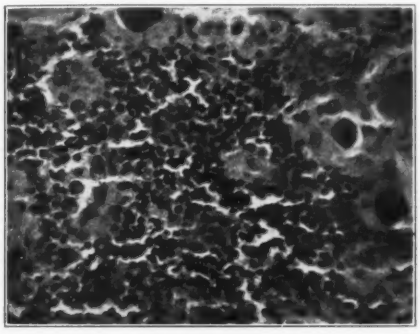

Fig. 4
Case 2. High power. Chronic thyroiditis (Riedel's struma type).

thyroid. It had grown slowly and at my examination the gland was large, nodular and more pronounced on the right side. There was some tightness in the throat at times and some palpitation of the heart. No tenderness nor areas of fluctuation were noted. The pulse was 88 and blood pressure 130/86. Basal metabolism test was reported plus 50 per cent and at another time plus 80 per cent. The Wassermann and Kahn tests were negative.

Pathological examination: A thyroid gland measuring 9 x 5 cm. On section the tissue had a light pink color, was firm, nodular and markedly fibrotic throughout. The fresh cut surface did not look like thyroid tissue. There were no cysts, no calcified areas and no evidence of any adenomas. The capsule was thick and fibrotic.

On microscopic examination, all sections showed a moderate number of small acini filled with colloidal material. There was a moderate increase in fibrous tissue and a marked lymphocytic infiltration with a number of lymph follicles and germinal centers. Areas of the sections showed a gland-like structure with very little fibrous tissue and no colloidal material. There was no pathological picture of tuberculous change (*Figs. 5* and *6*).

The diagnosis. Chronic thyroiditis of the Riedel struma type.

The three cases reported are unusual conditions and illustrate a type of thyroid pathology that has received careful study and thorough investigation by pathologists and surgeons during the past two decades. However, there are questions that are not answered and probably will not be until there is a more accurate method for tissue diagnosis. The histo-pathology in these cases is quite different from the usual microscopic findings seen in thyroid diseases. The first case in this series has most of the clinical findings and a typical microscopic picture of a Hashimoto's struma lymphomatosa. However it was not suspected by the surgeon and therefore was not diagnosed before the operation. The microscopic interpretation of the tissue removed is the only sure method of making this diagnosis. The second case presents quite a different picture from the first one. The clinical and microscopic findings are

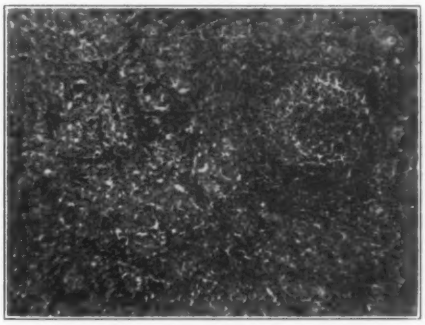

Fig. 5
Case 3. Low power. Chronic thyroiditis (Riedel's struma type).

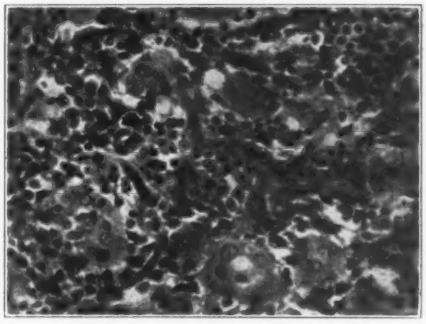

Fig. 6
Case 3. High power. Chronic thyroiditis (Riedel's struma type).

typical of the cases reported in medical literature as Riedel's struma. This was the pre-operative diagnosis and after a careful microscopic study of the tissue the diagnosis of chronic thyroiditis, Riedel's type, was made. The third case of the series is the most interesting and we believe a very difficult case in which to make an accurate diagnosis, as the clinical findings and the microscopic picture are in no way typical of either Hashimoto struma or the Riedel struma type. After studying a large number of the serial sections and comparing the microscopic findings with the previous cases we feel that the findings are very suggestive of an intermediate stage of the two diseases and that the pathological findings in this case are in many ways similar to those found in typical cases of Riedel's struma. We believe that the borderline cases studied clinically and microscopically at this stage of the disease lend support to Ewing's views of the disease, that Hashimoto's disease is an early stage of the Riedel's struma type and not a separate disease entity. The pathological changes are in keeping with the histological sequence which shows fibrosis following a chronic inflammatory change and a lymphoid cell infiltration of the tissues. Ewing has designated the condition as a "benign granuloma" in a number of his cases. Graham considers the two diseases as separate and distinct pathological conditions, one a general disorder with local manifestation in the thyroid and the other a local inflammatory change in the thyroid of an unknown etiology. It seems that to differentiate the two types would be impossible from the history, physical findings and symptoms and that the only clear cut differentiation lies in the histo-pathological appearance of the tissues. The most difficult group that the pathologist encounters is probably the phase that simulates the two types, or the so-called borderline type. However, we consider this an unsettled question in thyroid pathology and will wait for new developments in this field for future interpretation.

THE MALIGNANT GROUP

Malignant tumors of the thyroid gland are of the epithelial type in most cases and only those with wide experience ever see a malignant tumor of any other type. Pemberton reports four sarcomas in a series of 40,000 pathological examinations of the thyroid gland. Thyroid malignancy is a disease that is relatively uncommon. However, it is found in more than two per cent of all nodular goiters. Toland says that the incidence of thyroid malignancies is as high as 6.75 per cent; Pemberton, 2.7 per cent, and in our series of 60 pathological thyroids we found 6.6 per cent. This, we consider high for a non-goitrous region. However, our percentage should be lowered when we have a larger series to report. In 50 per cent of the thyroid tumor group, a clinical diagnosis of malignancy can be made with reasonable certainty. However, little can be done for the patient at this late stage. In the other 50 per cent there are no clinical signs or physical findings to make a differentiation between a benign and a malignant thyroid. How and when the malignant thyroid develops, is the most important question in thyroid pathology. However, it has been shown that 80 to 90 per cent of all carcinomas of the thyroid gland develop in pre-existing adenomas or nodular thyroids. The hyperplastic and colloid goiters very rarely show any malignant changes unless they have become adenomatous. A positive diagnosis of a malignant adenoma is exceedingly difficult in many of the nodular or adenomatous goiters, and the malignant area may be small and easily missed. For this reason this type of tumor sometimes gives rise to distant metastasis, when no primary tumor of the thyroid can be demonstrated. Then nodular goiters of long duration may suddenly increase in size and often the pathological lesions will show malignant and toxic changes. This was true in the first malignant case reported. The borderline group of thyroid diseases is often very difficult to clarify and wide experience in tumor pathology is necessary to make a diagnosis of the usual thyroid tumors seen in the average general hospital.

Case 4 (13,463).—Mrs. M. J., a white woman, aged 43, thin and emaciated, complained chiefly of goiter, which had its onset in November, 1934. At that time she noticed a small tumor mass in the neck which had shown a progressive enlargement. Physical examination showed a large, firm, nodular tumor mass, mostly on the right side and in the region of the thyroid gland. There was no history of goiter. The basal metabolism was reported as plus 50 per cent. There were no enlarged lymph nodes in the neck.

Pathological examination: Two large sections of the thyroid gland, 8 x 9 cm. and 6 x 4 cm., firm and nodular. On section the larger mass showed a large infiltrating tumor mass and small areas of thyroid tissue about the margin. The tumor growth was of a whitish color, soft and friable. The smaller specimen was of a dark red brown color, firm, and had the gross

appearance of hyperplastic thyroid tissue. There were no cysts and no calcified areas.

Microscopic examination: Sections from the larger mass showed an infiltrating epithelial growth with a gland-like arrangement of the epithelial cells. Areas showed mitotic figures and throughout the structure the cells were small and undifferentiated, an anaplastic type of cell. There was very little connective tissue and areas of the sections showed acini with some colloidal material. The sections from the smaller mass of tissue showed a variation in size and shape of the acini and a hyperplasia of the epithelial structure. One small malignant area was found in the tissue removed from the left side.

The diagnosis. Adenocarcinoma of the thyroid gland, Grade 3.

Case 5 (13,256).—Mrs. C. B. G., white, aged 42, complained chiefly of nervousness and a tumor mass in the neck. She had noticed a growth in the region of the thyroid for the previous three months, which had gradually grown larger. For the previous few weeks she had had difficult breathing. The pulse rate was 120. The basal metabolism test was plus 47 per cent. No enlarged lymph nodes were found in the neck. The blood iodine was 17.2 gamma per cent. Cholesterol was 151 mg. and serum calcium 10.5 mg.

Pathological examination showed two large sections of the thyroid gland, measuring 9 x 6 cm. and 9 x 5 cm. each, firm, slightly nodular and partially covered with a thick fibrous capsule. On section the cut surface presented a pinkish brown color and there was evidence of a moderate increase in fibrous tissue throughout the gland. There were no cysts or calcified areas and no normal thyroid structure was seen in the tissue removed.

Microscopic examination showed a general diffused epithelial growth with the formation of small gland-like structures and an increase in fibrous tissue throughout the sections. All sections showed a small amount of poorly stained colloid material and the acini were uniformly small. The epithelial cells were of the anaplastic type and showed marked proliferation (*Figs. 7* and *8*).

The diagnosis. Diffused adenocarcinoma of the thyroid gland, Grade 2.

The diagnosis of malignant tumors of the thyroid gland is not made any sooner than that of malignant tumors of the breast, as there are no clinical signs or symptoms which are positive and diagnostic in the early stages of the disease. We really see the end stage of the disease when the classical symptoms of thyroid cancer are present and at this advanced stage all forms of treatment are of little good. In 1934, Pemberton reported a large series of malignant thyroids (658) seen at the Mayo Clinic and in this series 38 per cent of the patients had inoperable malignant neoplasms when they were first seen. In the larger per cent of all thyroid tumors a careful histopathological study is required before a diagnosis can be made, and, even after that, to give an intelligent report on the borderline cases requires wide experience in thyroid laboratory. Neither the history, symptoms, nor physical findings will differentiate a benign from a malignant thyroid tumor. The so-called fetal adenomas are seen in a large number of thyroids and they are considered true benign neoplasms. However, this small nodular mass is often transformed into a malignant neoplasm. In recent years there has been an increase in thyroid cancer which has greatly interested the pathologist and the surgeon and as a result of their combined work, there has been a steady advancement in knowledge of thyroid disease.

SUMMARY

(1) Three unusual cases of thyroiditis, one struma lymphomatosa, (Hashimoto) and two cases of chronic thyroiditis, Riedel's type, have been reported and briefly discussed.

(2) Two cases of advanced carcinoma of the thyroid gland have been reported and discussed.

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UTERINE HEMORRHAGE IN LATE PREGNANCY*

By WILBUR E. HOFFMAN, M.D.
Charleston, West Virginia

Uterine hemorrhage in late pregnancy is one of the most formidable complications with which the practicing physician has to deal. We may classify it along with infection and toxemia to make up the three main causes of maternal death. Believing that the mortality rate is decreased or increased according to the judgment and skill of the accoucheur, good results depend on an early diagnosis and correct treatment.

Hemorrhage in late pregnancy is of serious nature and should be regarded as such until proven otherwise. The patient who is bleeding should be in a hospital for diagnosis and possibly treatment.

When bleeding comes from a placenta situated near the cervical os in a pregnant woman near term or in the last trimester of pregnancy, one has to consider placenta previa first. I wish to limit this discussion to those cases in which a definite diagnosis of placenta previa can be made.

In the last few years the practice of obstetrics has advanced and I believe physicians are paying more attention to ante-partum bleeding than before, although I recall two cases which resulted in maternal mortalities. A patient had a hemorrhage and was told that if it occurred again she would have to go to the hospital. The second hemorrhage occurred and the patient died on the delivery table from loss of blood following a version breech extraction. The second case had several hemorrhages and the physician insisted on her removal to a hospital, which was not done, and she died later. These cases illustrate the importance of an early diagnosis.

May I call your attention to the history: bleeding without pain, in the last trimester of pregnancy. Rucker has said: "A woman rarely bleeds to death from her first hemorrhage." Curtis says that the initial hemorrhage varies from a few drops to an exsanguinating flood, and in most cases the loss of blood amounts to a few ounces.

For an accurate diagnosis of these cases we usually rely on the history, observation that the head fails to engage and cannot be impressed into the lower uterine segment, and a digital examination. This latter may produce severe or grave hemorrhage or infection and lead to the death of the patient. Drs. Ude and Urner have reported thirty-five cases in which they were able to make a diagnosis of the various forms of placenta previa by a roentgenological study of the placenta. In our small clinic with the aid of our roentgenologist, Dr. V. L. Petersen, we have used their technic and have had very gratifying results. Ude and Urner recommend a Potter-Bucky diaphragm for taking the pictures. This is the more satisfactory method; however, an occasional patient presents herself after severe hemorrhage, when moving her is contraindicated. Using a portable x-ray machine, with the patient in bed, we have had good pictures of placenta previa. Following the technic of Ude and Urner, a catheter is inserted into the bladder, which is emptied, and about 40 to 60 c. c. of 10 to 12 per cent sodium iodide solution are injected. The amount of the instillation is only sufficient to outline the urinary bladder, the catheter being withdrawn before the roentgenogram is made. An anteroposterior film is made immediately.

We know that the pregnant uterus rests against the abdominal wall and displaces the omentum and intestines. The wall of the bladder is separated by two folds of the peritoneum. The total diameter of the soft tissues normally lying between the inner wall of the pregnant uterus in the third trimester of pregnancy and the lumen of the bladder on the roentgenogram is about 6 to 8 mm. in depth. Unless the presenting head is displaced upward by a solid mass or a placenta previa or blood clots from a premature separation of the placenta, the head lies invariably against the lower anterior wall of the uterus. Only after careful analysis of the densities between the bladder margin and the fetal skull do we depend on a roentgenologic diagnosis of placenta previa. This condition cannot be accurately diagnosed in cases of breech presentation or transverse presentation because the inner wall of the uterus cannot accurately be determined.

The normal placenta varies from 2 to 3 cm. in thickness and in low implantations is relatively thinner than normal since it spreads over a larger area. Because of poor blood supply of the lower uterine segment, it takes the shape of the uterine wall externally, and because of the pressure of the amniotic fluid and fetus internally, it is convex outwardly and concave in-

*Read in Section on Obstetrics, Southern Medical Association, Twenty-Ninth Annual Meeting, St. Louis, Missouri, November 19-22, 1935.

Fig. 1
Patient with a normal pregnancy in the last trimester. There is a small soft tissue space between the fetal head and bladder.

wardly. A visible mass seen between the fetal head and the urinary bladder along with the history gives a typical picture of placenta previa.

I should like to report four case histories of this condition which were diagnosed by x-ray.

Case 1.—Miss L. G., 24 (para 0), gravida 1, gave her last menstrual date as October 5, 1934. She was admitted to the hospital on May 25, 1935, and gave a history of slight bleeding without pain each day during the previous month. She had received no prenatal care. Examination revealed pregnancy of approximately eight months. Rectal examination revealed an undilated cervix with boggy mass between the presenting part and the examining finger. On May 27, roentgenological findings showed increased space between the bladder and fetal head, indicating placenta previa. On May 30 cesarean operation was performed and a living baby delivered. The placenta was found in the lower uterine segment covering the cervical os.

Case 2.—Mrs. K. R., aged 20 (para 2), gravida 3, had her last menstrual period November 1, 1934 Pregnancy was normal until 5:00 a. m. July 3, 1935, when she awoke and found that she was bleeding moderately from the vagina. While she was in bed, without pain, bleeding became more profuse. Her physician brought her immediately to the hospital, a distance of some 40 miles. She was given fluids and an x-ray examination was made which revealed several centimeters separating the head of the fetus from the bladder, indicating the presence of a placenta previa. Cesarean section was performed with the delivery of a living baby. The placenta was attached to the lower uterine segment, covering the internal os.

Case 3.—Mrs. B. B., aged 31 (para 2), had her last menstrual period February 1, 1935. Pregnancy progressed normally until the morning of November 4, when she called me at about 7:30, saying she was bleeding without pain. She was immediately sent to the hospital. Examination revealed a pregnancy at term. The baby was in the left occipito-anterior position, fetal heart rate 156 and head floating. There was a moderate amount of bleeding which had soaked six pads from the beginning of the hemorrhage until I saw her at the hospital. X-ray examination revealed a mass separating the top of the bladder from the fetal head. No vaginal or rectal examinations were made. Immediate cesarean showed a placenta attached to the lower uterine segment anteriorly and covering the entire internal os. A living female baby weighing 8 pounds 3 ounces was delivered.

Fig. 2
Case 1. There is a wide space between the fetal head and bladder margin, showing a placenta previa. In this case the baby was premature.

Fig. 3
Case 3. Note the soft tissue mass between fetal head and upper margin of the bladder. (Central type of placenta previa.)

Fig. 4
Case 4. Note the wide margin of separation between fetal head and margin of bladder. (Central type of placenta previa.)

Case 4.—Mrs. E. C., aged 29 (para 5), had her last menstrual period February 6, 1935. On November 24, 1935, she awoke and found she was bleeding from the vagina. On November 25, she was sent to the hospital, a distance of some fifty miles. Examination revealed a pregnancy at term, profuse vaginal bleeding and no pain. X-ray examination showed a mass separating the bladder from the fetal head. No vaginal or rectal examinations were made. Immediate cesarean showed the placenta in the lower uterine segment entirely covering the os. A living male baby weighing eight pounds two ounces was delivered.

We believe this method of diagnosis of placenta previa will decrease the possibilities of infection by limiting the vaginal and rectal examinations.

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DISCUSSION (*Abstract*)

Dr. Wm. H. Vogt, St. Louis, Mo.—I claim no practical experience with this method.

The diagnosis of the location of the placenta with x-ray was done in 1930 by Menees, Miller and Holly. They injected a solution of strontium iodide through the abdominal walls directly into the amniotic sac and in that way changed the amniotic fluid into a contrast material in which the placenta and the soft tissue of the fetus were demonstrated as filling defects. This method proved to be dangerous to the fetus and resulted in a number of instances in premature delivery. Later Kerr and Mackey modified this method by substituting a derivative of iopax for the strontium iodide. This solution was found to be non-toxic and non-irritating, but the injection likewise had a great tendency to terminate pregnancy.

In 1934, Snow and Powell were able to show the outline of the placenta in normal implantation without injection of any contrast material into the amniotic fluid. They had not used this method for the study of placenta previa, but their method was without any danger either to the fetus or mother.

When Menees, Miller and Holly first published their report, I dismissed the subject from any further consideration, because I could see no reason for going to all this trouble and putting the patient to the extra expense of x-ray examination. I have never considered it especially difficult to make a diagnosis of placenta previa by the ordinary clinical methods.

From the pictures which Dr. Hoffman showed I should not be willing to make a definite diagnosis of placenta previa without other clinical evidence. I believe one could be equally sure of one's diagnosis by rectal or vaginal examination, which, after all, are not serious when done with proper precautions.

I note, too, that because of the diagnosis of placenta previa the operation of cesarean section was done in each case reported here today. No other indication for this operation was given except that placenta previa was diagnosed by the x-ray and there was no other examination made of the patient. I should want more evidence than is here presented before I should be willing to operate.

Likewise am I opposed to doing cesarean section for this condition except in rare instances. Statistics from clinics in which such cases are treated by conservative methods show a much lower mortality than do those in which radical methods are practiced. There cannot be much argument about this. While I know full well that many obstetricians favor this procedure, I am of the opinion that the advocates of this operation fail to realize that three important factors must be considered in the management of such cases. (1) For the most part these patients are seen when infection has either occurred or is likely to occur; (2) the fetus is already jeopardized by the maternal bleeding; and (3) the fetus is in a great number of cases so premature that it can never bear the vicissitudes of extra-uterine life. The mortality rate is high because of the actual or potential infection and the fetal mortality is high because of the great maternal blood loss and prematurity.

Any method, however, regardless of its cost, which will help us to make a clearer and more definite diagnosis of this serious condition should receive our most careful consideration, and I shall follow with great interest any further development along these lines.

Dr. W. B. Anderson, Nashville, Tenn.—The two main points brought out in Dr. Hoffman's paper are diagnosis of placenta previa by x-ray and indication for cesarean. A soft tumor of the cervix might have given the same result in his x-ray picture, but since hemorrhage from the uterus, without pain, at that time of pregnancy is almost pathognomonic of placenta previa, I think he was justified in his diagnosis. However, I should not have been satisfied without a vaginal examination to classify the extent of the placenta previa. All placenta previas should be in a hospital where

they can be prepared for a vaginal examination. One vaginal examination, properly made, does no harm. A lateral placenta previa may give you the same x-ray effect and be more safely delivered *per vaginam*.

Dr. Hoffman (closing).—I am not recommending cesarean section for the treatment of placenta previa. For patients who give a history suggesting placenta previa, may I recommend this method of diagnosis, provided you have a competent roentgenologist. It should decrease the possibilities of infection and hemorrhage by limiting the vaginal and rectal examinations. By using this method of diagnosis, we have not caused any undue bleeding.

THE MANAGEMENT OF URETERAL CALCULI*

By Roy J. Holmes, M.D.
and
Milton M. Coplan, M.D.
Miami, Florida

Urologic literature during the past few years has offered many splendid papers on the subject of ureteral calculi. In our locality there is a relatively high incidence of uro-calculosis, and we have seen many cases. We present this subject not with the idea of offering any new concepts regarding ureteral calculi, but with the belief that we may help to crystallize some of the more important ideas concerning a rational attack on ureteral lithiasis.

Although the scope of this paper does not embrace the diagnosis of ureteral calculi, there are certain diagnostic considerations which play a definite part in the proper management of the clinical case. For this reason we must first evaluate the diagnostic data, as they form a foundation for the support of our ideas on the subject.

A complete history is of inestimable value. The patient suffering from an initial attack of renal colic is cared for much more conservatively as a rule than the patient who gives the history of a series of prolonged attacks of acute ureteral blockage. Those who consult us with recurrent ureteral stones, if properly questioned, can supply us with a history of the ease or difficulties with which the previous stone was passed or extracted, and with this information we can more readily decide on a method of treatment adaptable to the particular patient.

Much depends upon the physical findings in every case and we warn against the tendency of depending too much on skillful use of the cystoscope while but little time is spent in the examination of the general condition of the patient. The toxic appearance which some of these cases present can never be seen transvesically. Laboratory data, therefore, become of vital aid in the intelligent handling of every case. The degree of obstruction may appear very slight when, with a catheter successfully passed beyond a ureteral stone, it is found that the kidney pelvis contains a nominal amount of residual urine, and yet by determination of the blood retention of nonprotein nitrogen or urea, we may learn that this patient is far more ill than we had suspected.

Clear x-ray films which show the exact position of the stone, its approximate size, as well as its contour and its alignment in the ureter are the urologist's best friends. Smooth stones of a rather large size will quite often pass spontaneously, whereas a rather small rough, spiculated calculus cannot be dislodged even with the greatest dexterity on the part of the instrumenteur. A small triangular stone aligned with the apex downward may offer great difficulty, whereas a larger stone of the same shape with its base presenting, may pass very readily down the ureter. When possible we should obtain from our x-ray study the approximate size of the kidney on the affected side and determine the degree of enlargement, if any, by comparison with the kidney of the opposite side. Any appreciable increase in the size of the kidney affected would naturally indicate the need for more urgent measures for relief of the obstruction.

We do not believe, as do some, that the presence of stones in both ureters or in one ureter and one kidney pelvis seriously alters the choice of procedure. This condition merely calls for a decision as to which side is most seriously affected. When the obstruction is bilateral surgical intervention should not be delayed. We believe that it is infinitely better to release back pressure on both kidneys simultaneously than to hope that one kidney will in some miraculous manner withstand the obstruction for a period of five or six days longer while the other is recuperating from adequate surgical drainage. Situations such as this require urologic judgment more than surgical skill, although the latter attribute is ever welcome.

Since the urinary tract is not uniform in every individual, it is quite essential to determine as early as possible if there is any variation from

*Read in Section on Urology, Southern Medical Association, Twenty-Ninth Annual Meeting, St. Louis, Missouri, November 19-22, 1935.

the normal in patients suffering from ureteral calculi. Stenosed ureteral orifices, ureteroceles, congenitally narrowed ureters, such as are often found in pelvic and ureteral reduplications, definitely increase the difficulty of successful spontaneous passage or instrumental extraction of stones. If we are acquainted with such anomalies at the outset, many hours of suffering and the increased hazard of tissue destruction may be prevented. In the renal anomalies such as horseshoe kidney, dystopias and ectopic kidneys, the formation of urinary calculi is quite common. Therefore, while one is evaluating all of the factors present when considering the suitable method for handling obstructing ureteral stones in these conditions, he must first have thoroughly satisfied himself as to the congenital variations present.

Relief from pain is the patient's primary thought and while ever willing to provide that relief when possible, we, as urologists, have a keener consideration for the destructive effect upon the embarrassed renal tissue. We must be guided in our decisions by the systemic complications that are present or that can beset the patient, for total urinary suppression, even when only one kidney is obstructed, must ever be borne in mind. Bacterial invasion of the blood stream may suddenly appear and produce rapid death, although up to the time of its appearance the patient's general condition might have been very satisfactory. We have in our records two cases of death due to blood stream infection with *Streptococcus hemolyticus* only because these patients' stones were so small and so easily manipulated that we forsook surgical interference, hoping to extract the stones by what seemed to us more conservative measures.

It has been our observation that morphine is not the only drug that will give relief from pain in ureteral obstruction. Where there are no reflex gastro-intestinal symptoms, especially vomiting, it is wise at times to employ some drug other than morphine with the hope of getting better relaxation. We have found some of the barbiturates especially valuable in this respect and have administered them intramuscularly when they could not be taken by mouth. When, however, morphine is used, atropine sulphate should always be incorporated with it. The work of Ockerblad has conclusively shown that morphine actually increases the muscular contractions of the ureters, while atropine sulphate acts to paralyze the smooth muscle comprising the ureteral wall.

At this point we should like to digress for a moment to mention the use of ephedrine for this same purpose. We have used it on a number of occasions and it appears not only to produce the same effect on the smooth muscle of the ureters as does atropine, but acts more rapidly and more profoundly. Benzol benzoate and its associated drugs have, in our hands, shown no demonstrable results.

Hinman, in his splendid text, "The Principle and Practices of Urology," has so concisely grouped the procedures involved in the removal of ureteral stones that we quote from his work:

"The treatment of ureteral calculus is: (1) expectant; (2) urological; (3) surgical."

With such a classification it does not mean in every instance that these three phases of procedure must be used consecutively. It is not infrequent after an analysis of the history and study of the roentgenograms and laboratory data that we dismiss the first two procedures immediately and advise surgery as the conservative method of choice.

Expectant treatment, which implies watchful waiting for spontaneous delivery of the stone and urologic instrumentation, is frequently carried far beyond the limits of safety to the patient. If renal colic continues for twenty-four hours after the onset of an attack, regardless of the severity of the colic or of the size and position of the stone, a catheter should be passed beyond the point of obstruction if possible in order to release the affected kidney from its damaging back pressure. It has been our observation that small stones, if left unmolested for several days, insidiously produce sufficient edema of the ureteral tissue surrounding them to render the successful passage of a catheter impossible, whereas the obstruction might easily have been surmounted had the edema not progressed too far. When following the expectant course the natural influences should be supported as much as possible. Quantities of water should be given the patient and atropine sulphate or ephedrine at intervals will do much to relax the ureteral musculature.

Instrumental extraction of ureteral stones introduces a phase of the subject about which much has been written and for which many devices have been offered. The one rule, which we believe irrevocable and which we consider in all cases, is that the instrument used must be sufficiently small either to pass beyond or at least alongside of the stone with not too much danger of perforating the ureteral wall, and it must be durable. Numerous forceps, snares, and

the basket type extractors have been devised, but unfortunately they are usually so large in caliber that it is on rare occasions that they satisfy the first requisite of this rule; or they are so frail in construction that they fall far short of meeting the requirement of durability, and their use is fraught with danger. In the upper third of the ureter not one of these instruments is applicable. Fortunately, not many stones "hang" or become impacted in the middle third of the ureter so that one might conclude that the various extractors can be used only in the lower third of the ureter. Regardless of the design, we believe that most of these instruments offer definite hazards.

It is our opinion that the safest and most uniformly applicable stone extractor is the ureteral catheter assisted by such instruments as are normally employed to dilate the ureter or enlarge an ureteral orifice. The many suggested applications of the ureteral catheter are too numerous to do other than mention at this time. Spiraling the catheter as it is withdrawn, injection of oil at the site of the stone through the catheter, the quick jerk upon withdrawal with the idea of spontaneously pulling the stone downward, the use of multiple catheters to form a mesh, if and when several can be simultaneously passed behind the stone, are but a few methods that have been proposed and used with varying success. Once successful in surmounting an obstructing stone with an ureteral catheter we leave the catheter in position for at least twenty-four hours. The ureteral peristalsis against the catheter gives an added impetus to the propulsion of the stone, while at the same time the impaired kidney is being comfortably drained and protected against serious injury.

We have recently devised a method whereby this same ureteral catheter is employed to make a loop behind the stone and, in our hands, has been quite successful. Before describing the procedure we should like to emphasize that it is not altogether free of theoretical disadvantages, but in practice we have had but one occasion to regret its use and this we shall reveal in due course. It occurred to one of us that if a number 5 or 6 catheter could be passed successfully beyond an ureteral stone and into the kidney pelvis and if there were some way of reversing its course so that it could again be brought down, the ureter producing a sling or loop at the superior pole of the stone, that by gentle traction of the sling against the stone the calculus could be dragged from its position in the ureter downward into the bladder.

We realized that where stones were obstructing the ureter there was necessarily some degree of urinary retention behind it, which at least caused both the ureter and kidney pelvis above it to remain open if not actually distended. This we believed would make the turning of a catheter possible if we had a means of turning it. We therefore selected an ordinary silk fiber shellacked whistle-tip catheter, to the tip of which is attached a strong linen thread. The method of preparing this is illustrated in *Fig. 1.*

We use this method so as to avoid making a knot at the tip of the catheter which would naturally increase its caliber and add to the difficulty of passing it beyond the stone. Using an operative cystoscope with a double channel we

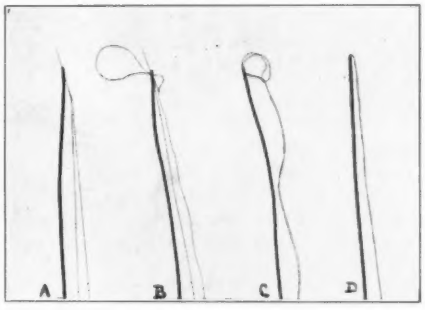

Fig. 1
Illustrating the method of anchoring linen thread through the terminal eyes of the catheter so that the thread comes off the tip of the catheter without making a knot.

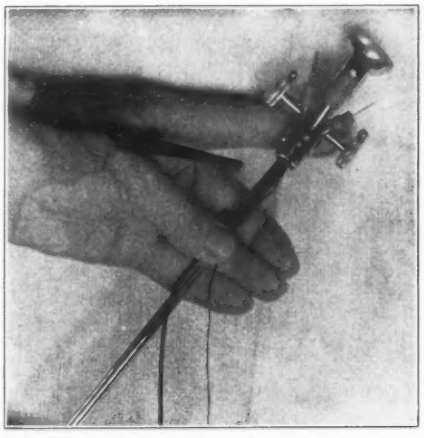

Fig. 2
Illustrating the method of assembling the catheter and thread into the operating telescope by the retrograde method.

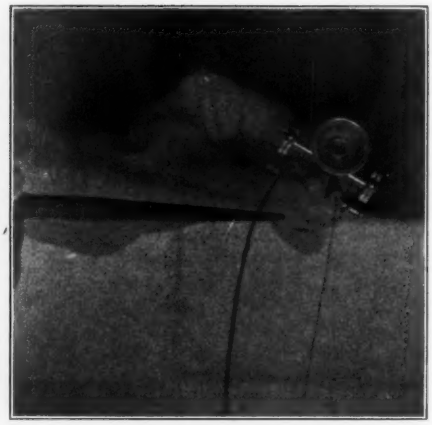

Fig. 3
Showing the catheter and thread assembled in separate channels which facilitates independent manipulation of either part.

place the catheter in one channel and the thread through the opposite one (this is done by the retrograde method as shown in *Fig. 2*) for the reason that it permits the operator to keep the thread from falling into close contact with the catheter (*Fig. 3*) and also enables the operator to control both the catheter and the thread independently during the process of reversing. If we are successful this catheter arrangement can be passed by the stone with the thread attached with little more difficulty than a catheter alone would cause. Once beyond the stone the catheter is passed all the way to the kidney pelvis (*Fig. 4*). With the catheter held in place gentle traction is then made on the string, which turns the tip downward and starts its passage into the ureter (*Figs. 5-A* and *B.*)

It is evident that the kidney pelvis actually serves as a "turning basin" for the catheter tip and we stress this because to turn the catheter at any level in the ureter would undoubtedly result in trauma to the tissues. With the catheter still held firmly the catheter tip is pulled down the ureter beyond the stone, thereby producing a definite loop or sling above it (*Fig. 6-A*). From this point it is wise to pass the catheter an inch or two higher for every inch or two that the string is withdrawn. The catheter tip is brought farther down until it comes into view in the bladder, and it should then be drawn into the sheath of the cystoscope so that once the traction is established the blunt tip will not denude the mucous membrane of the bladder. In this way the sling gradually closes in completely on the stone as shown in *Fig. 6-B*. With the cystoscope in position the traction can be made under observation and should the loop slip over the stone the catheter can be re-introduced and a second attempt made to engage the stone in the loop. We have succeeded in removing a sufficient number of stones with this method to convince us of its practicability and in no case has it caused serious trouble. *Figs. 7* and *8* show stones engaged in the catheter loop prior to extraction.

In one instance after engaging the loop around the stone we found that by traction we could dislodge neither the stone nor the catheter. After many anxious moments we decided to leave the catheter in position and remove the cystoscope. The patient was put to bed with continuous traction applied to the conjoined ends of the string and catheter, and atropine was administered hypodermically. Within a short time the catheter pulled out and with it came the stone into the bladder. It has occurred to us that if in the future this same situation should arise, we might administer a small amount of spinal anesthesia and then resume our traction.

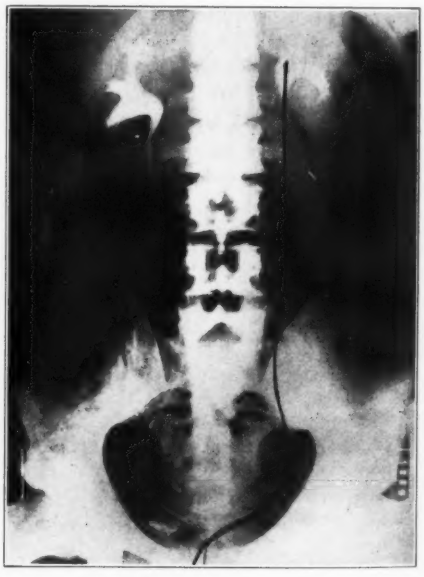

Fig. 4
Showing the threaded catheter passed to the kidney pelvis. (Composite illustration made by super-imposing catheter on an x-ray film of bilateral pyelogram).

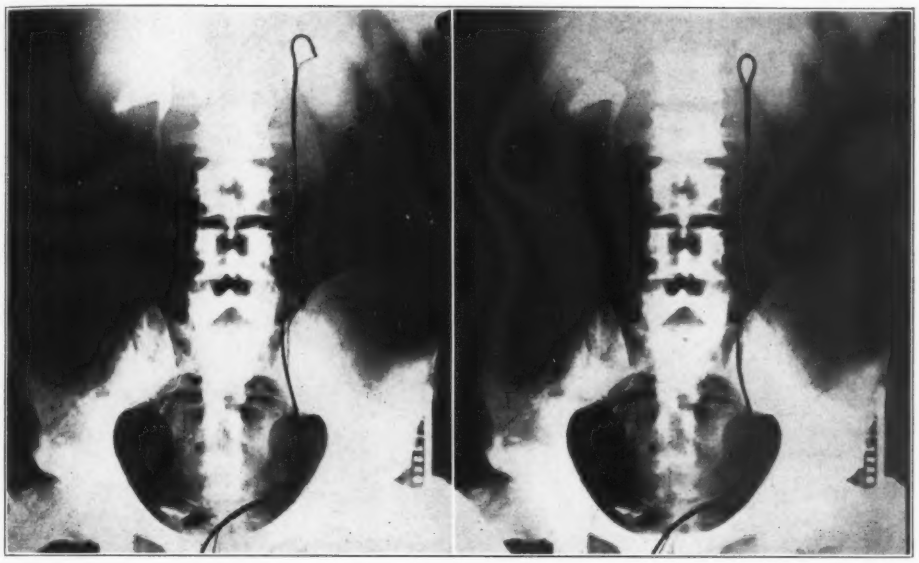

Fig. 5-A
Showing the catheter beginning to turn in the kidney pelvis after traction is applied to the thread (composite illustration).

Fig. 5-B
Showing catheter loop completed with the distal end being brought down the upper third of the ureter (composite illustration).

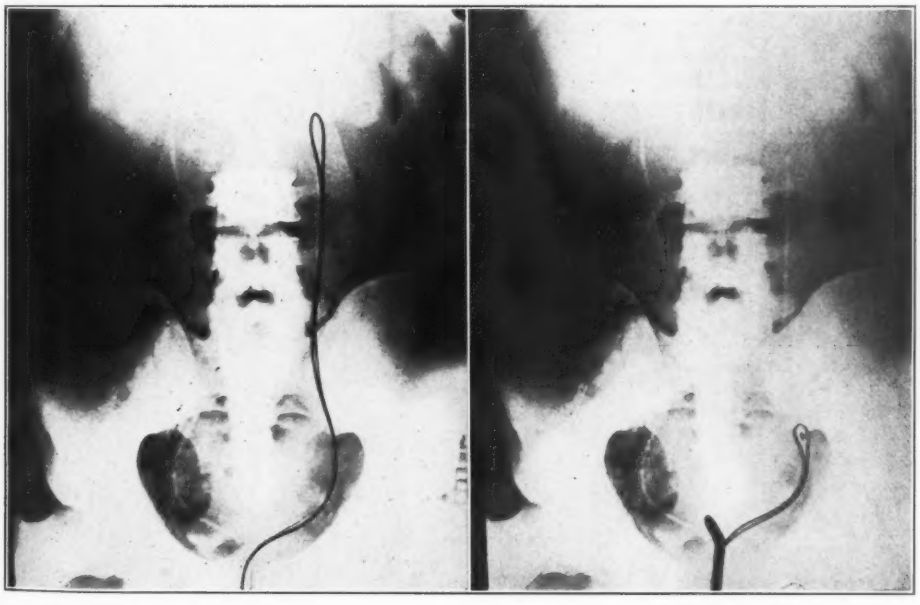

Fig. 6-A
Showing a further advance of the loop down the ureter (composite illustration).

Fig. 6-B
Showing catheter loop brought down to a point where it now encircles the ureteral calculus (composite illustration).

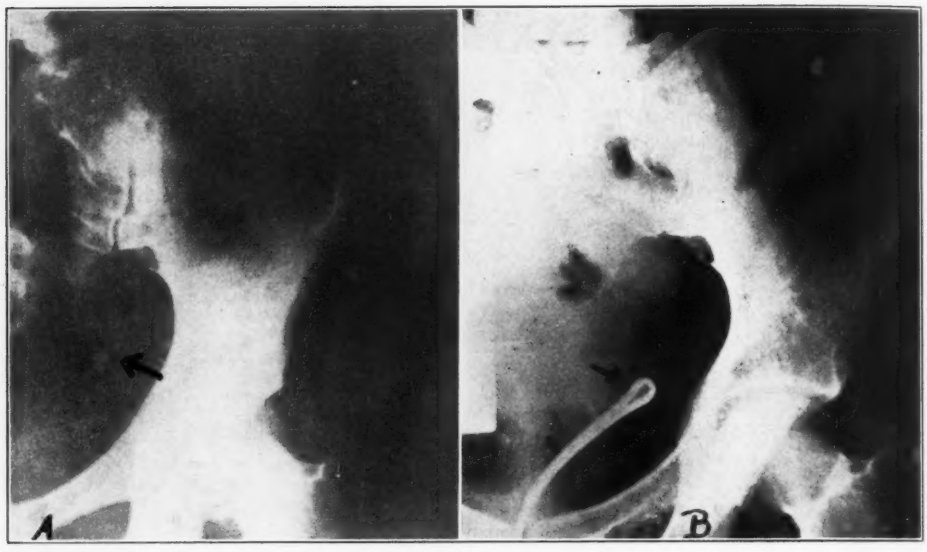

Fig. 7
Actual x-ray. A shows stone in lower third of ureter. B shows stone caught in catheter loop.

While this method has resulted in no serious embarrassment to us, we have made it a point to warn either the patient or his family of the possibility of the catheter's becoming lodged in the ureter. We have in most instances used the procedure only when other methods have failed to release a stone and therefore it has been easy to explain to the patient that if it should not work, surgery will be necessary regardless.

Throughout our thesis we have expounded the doctrine of conservatism and precision. The foregoing description of a method of extracting ureteral stones we sincerely believe falls within the category of conservative procedures. We wish at this time to describe briefly another simple means of removing stones from the lower segment of the ureter in females, which has been made possible with the advanced development of the ocular system in the McCarthy foroblique and direct vision telescope. The procedure as we describe it may seem to you highly radical, but we assure you it is essentially a harmless method. We reported this technic in a paper which appeared in the *Florida State Medical Journal* in 1931, and since that time have used it with success on a sufficient number of occasions to warrant describing it to you.

First the urethra is thoroughly dilated. About three inches of open-end soft rubber catheter are passed into the urethra, the bladder is filled with fluid, and through the catheter the telescope of the McCarthy panendoscope or McCarthy routine cystoscope is introduced into the bladder. The rubber catheter which has acted as a urethral shield is then withdrawn (hanging loose at the proximal end of the telescope), leaving the telescope in place. A thin blade uterine dressing forcep is passed through the urethra

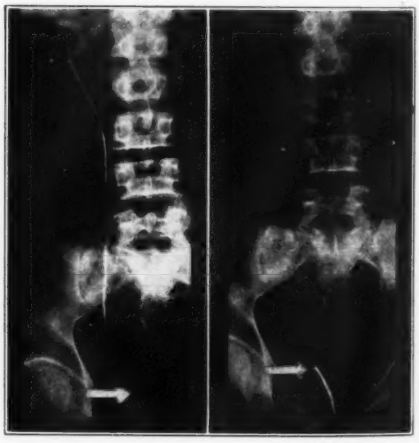

Fig. 8
Another x-ray showing stone engaged in catheter loop.

Fig. 9
Illustration depicting observation telescope in bladder and forcep engaged in lower ureter.

alongside of the telescope. Under vision the forcep can be introduced into the ureter and up to the stone. With this accomplished, the telescope is removed, the forcep opened slightly until the stone engages, and then holding the stone firmly, it is withdrawn into the bladder (*Fig. 9*).

When stones become impacted in either the upper or lower third of the ureter, on many occasions we have been able to save the kidney great damage by pushing the stone back to the kidney pelvis by the force of an ureteral bougie. In employing the bougie we take the blunt end, which has previously been sand-papered to smoothness, and actually lift the stone upward. It is far better in our opinion to do this even though it means a recurrent attack of colic than to permit the kidney to remain subjected to extreme back pressure. This is especially applicable when it is practically assured that surgery will be inevitable. As previously mentioned, a stone might easily impact itself in the ureteral lumen when it engages the canal in one position, whereas if allowed to re-engage the ureter in another alignment, it will move easily downward.

When dilatation of a segment of ureter is advisable in order to facilitate passage of a small stone we have made it a practice to dilate only to the position of the stone and make no attempt to pass beyond it. It is not unlikely that projecting edges of a spiculated stone might be forced through the mucous membrane, thereby producing a portal of entry for bacterial invasion into the lymphatics, if large bougies are introduced and become wedged tightly between the stone and ureteral wall.

If it is decided that surgical removal is the method of choice it is but natural that the site of incision must depend on the position of the stone. With the stone in the upper third or middle third of the ureter a low kidney incision with an extra-peritoneal approach to the ureter is the method of choice. When possible we never disturb the kidney from its bed, but rely entirely on our ability to find the ureter and by gentle palpation trace the course of the ureter up or down to the site of the stone. In order to facilitate this we determine from our x-ray studies the exact position of the stone in relation to the transverse processes of the vertebrae, and our standing order is for a flat kidney-ureter-bladder film just before the patient is operated upon. Once the stone is found, it is held firmly while the ureter is gently freed for a slight distance above and below the stone. Narrow ribbon tapes are then passed under the ureter both above and below the stone and the ureter is suspended. These tapes also serve to hold the stone so that it cannot move away from the site of exposure. The usual longitudinal incision is made over the stone. There was a time when we felt that these incisions should be left open both for drainage and because of a resultant narrowing of the ureter at the site where sutures were placed. But with the introduction of a special ureteral suture, which is attached flush on the distal end of a small curved needle, we have found that the closure of these incisions is much more easily obtained without consequent trauma and that the period of convalescent drainage is definitely reduced. It is our rule to place two interrupted sutures to the half inch of incision and care is taken that the suture introduced does not include the mucous membrane. A cigarette drain is always carried from the ureteral incision to the flank. When this procedure of closing the ureter tightly is followed it means that within a period of ten days or two weeks a catheter should be passed up the ureter to determine patency and if necessary to lavage the kidney pelvis. Needless to say, this does not threw an additional burden on the patient's recuperative faculties.

In cases where stones are obstructing the upper third of the ureter just below or in the uretero-pelvic junction, in which the kidney pelvis is of the extra-renal type, we have, whenever

possible, made our incision into the renal pelvis in a line parallel to the ureter and with a small grasping forcep extracted the stone. We believe that this approach certainly has its advantages over the direct incision into the ureteral lumen for there is no chance for consequent ureteral narrowing.

For stones situated in the lower third of the ureter a surgical approach must be selected after careful determination of the exact position of the stone. If it is located above the intramural or terminal inch of the ureter, we prefer an oblique incision parallel to but slightly higher than the inguinal incision under a spinal anesthesia. We do a muscle spreading dissection and find that we have what we believe to be the ideal exposure. The lateral rectus incision and McBurney incision do not give quite so direct an approach to the lower ureter as does this incision.

When surgery is necessary to remove stones from the terminal inch of the ureter we believe, as does Hinman, that the suprapubic midline approach is far superior to any other. Through this entrance the bladder is easily deflected and the peritoneum stripped away, making this portion of the ureter more accessible. This, however, is one of the most difficult operations in urology and requires extreme skill because of the depth of the cavity in which one must work. In this respect intelligent surgical assistants, who are acquainted with every step of the procedure, are of extreme value. Only the operator can get the stone, but his assistants, by their knowledge of retraction and exposure of tissues, make it possible for him to do so. On several occasions where a stone in this position could not be reached we have not hesitated to open the bladder through a midline incision, locate the orifice of obstructed ureter and then cut down directly over the stone, being careful to have our incision go only through the tissue of the bladder and anterior ureteral wall at that point. It is quite amazing the ease with which stones impacted in the intramural portion of the ureter can be removed in this way. This procedure is equivalent to a ureteral meatotomy done with ureteral scissors through the cystoscope, the advantage being that the bladder can usually be pushed upward by a hand that has been passed down behind it, and that the stone can actually be cut down upon. The closure of this incision is precisely that of the upper ureteral incision. It heals without difficulty.

We have said nothing about the complications arising from a long standing ureteral obstruction, which has a serious effect upon the kidney. These complications must be considered when surgical methods of removing ureteral calculi are carried out. The large pyelonephrotic sac which not infrequently develops had best be removed as a uretero-nephrectomy if the opposite kidney is of good function and there is no previous history of calculi in that side. It has been our custom to evaluate degrees of pyelonephrosis on a basis of a 1, 2 and 3 grading, and we have in recent years followed the principle of permitting the first and second degree types to remain within the body: for a large majority, after the obstruction is released, will return to a surprisingly good functional state.

In third degree pyelonephrosis, however, kidney tissue has been destroyed to such a degree that even though a small amount of urine is secreted, the kidney serves only as a permanent source of infection if allowed to remain.

In large hydronephroses we make no attempt at plastic repair of the renal pelvis, if we are successful in extricating the stone and assuring ourselves of adequate downward drainage. Where we encounter a very small ureter or believe that the peri-ureteral inflammatory process at the site of an impacted stone may be sufficient to interfere with good drainage, we introduce a small two-winged catheter through a nephrotomy stab to the kidney pelvis to provide for drainage until the aforementioned ureteral inflammatory process can subside. It has been our experience that a small ureteral catheter passed through the ureteral incision and upward to the kidney pelvis with its lower end brought out of the wound, acts only to increase the inflammatory process in the ureter, and certainly it has on several occasions facilitated the formation of permanent fistulous communications between the site of the ureteral incision and the flank. In every case of open operation for ureteral calculi we place one or more cigarette rubber tissue drains in the wound down to the draining point, being careful that the proximal end of the drain does not lie too close to the line of incision, for here again we believe is a frequent cause for fistulous formation if the end of the drain becomes adherent at the site of the ureteral incision.

DISCUSSION (*Abstract*)

Dr. Bransford Lewis, St. Louis, Mo.—In discussing and promoting the cystoscopic removal of ureteral calculi, following the presentation in 1904 of my cys-

toscopic equipment of ureteral dilators, forceps, scissors, orifice incisors, I have invariably insisted that opportunity for passage of the stone down the ureter should be provided by preliminary dilatation of the canal before using a tractor for direct removal. This sequence must always be followed or, without doubt, the operator is putting the cart before the horse and paving the way to trouble for himself and his patient. With this proviso strictly adhered to, the cystoscopic method of removal is permissible, and when successful is eminently more satisfactory to the patient than being cut open for the removal.

Dr. Otto J. Wilhelmi, St. Louis, Mo.—Dr. Coplan's bougie is ingenious and the subject is of especial interest to me, for in the past month I happen to have had, at the same time, four ureteral calculi, all of them impacted.

No matter how grossly our symptoms and urinary findings point toward stone, we are never justified in rendering an accurate diagnosis without the assistance of x-ray and retrograde catheterization; and we must also remember that over 5 per cent of all stone shadows are invisible to x-ray.

I have recently seen a patient with symptoms and x-ray evidence of stone. Meticulous investigation revealed a salpingitis which pressed on the ureter, causing a periureteritis and blockage of the renal pelvis.

In another treated case, x-ray showed the stone engaged in a spiral steel bougie which would lead one to believe that its removal was assured. However, it escaped in the manipulation and slid back into the kidney pelvis when the patient was placed in Trendelenburg position. This was one of those migratory stones that Dr. Bransford Lewis wrote about and which he demonstrated could be removed by manipulating the patient in extreme Fowler's position. After three weeks of various attempts I finally did a ureterotomy and removed this stone with comparative ease, the patient leaving the hospital seven days after the operation.

In cases of impacted ureteral calculi, after three unsuccessful attempts at release, the advisable procedure is ureterotomy. If the stone lies very low in the ureter, near the vesical orifice, it is advisable to push it up near the iliac spine and to go in from this point. Using a right rectus incision, the operation is not difficult, and the opening in the ureter should be made just above the area where the stone has lodged to avoid future stricture formation.

This procedure is more advisable than repeated cystoscopic attempts, which often result in serious trauma and irreparable kidney destruction.

Dr. Coplan (closing).—Respect for urinary tract tissue is absolutely essential in any method employed for the removal of ureteral stones.

If one advises against the passage of anything behind a stone, he is perhaps leaning a little further toward the conservative side than is necessary. The method which we have described certainly has its theoretical dangers. On the other hand, they do not seem to manifest themselves when the method is carried into practice. If a catheter should break, you will agree that we still have both ends of it under our control so that the two sections can be pulled down without much trouble. Certainly the small loop formed by the reversing of the catheter does not dilate the ureter beyond physiologic and anatomic limitations.

In closing, may we emphasize to those who attempt to use the catheter loop that they will encounter, first of all, difficulty in passing it by many stones, just as they would find it impossible to pass an unthreaded catheter behind a stone. Until the technic is fairly well developed manipulation of the catheter in the process of turning it will be an awkward step.

CUTANEOUS LYMPHOBLASTOMA: SOME REMARKS ON ITS TREATMENT*

By JACK W. JONES, M.D.
and
HERBERT S. ALDEN, M.D.
Atlanta, Georgia

As a clinical concept, there is perhaps a no more ill-defined dermatologic condition than that known as "lymphoblastoma of the skin." This term, considered as it must be as all inclusive, straddling the many gaps in the knowledge of the pathology of the lymphatic system, does not delineate any well defined clinical syndrome nor any set pathologic process. Add to such an expansive term the protean character of its dermatological manifestations and one is not surprised at its lack of definition. So we must come to think of the term "lymphoblastoma" as broadly generic and considered as an effort to flee from the "tyranny of words" so aptly discussed in a recent communication by Williams.[1]

Gathered under the broad skirts of lymphoblastoma of the skin are the leukemic infiltrations, Hodgkin's disease, mycosis fungoides, generalized exfoliative and edematous eruptions associated with lymphoid hyperplasias of the blood and lymph nodes, myelogenous leukemias and various bullous, ulcerative and nodular eruptions associated with leukemia. It is obvious that in many instances the dermatologic appearances are merely one clinical outlet of a deranged hemopoietic system, and, as such, frequently represent the first clinical and pathological evidence of disease. There are a few cases (particularly the clinically unidentified generalized exfoliative eruptions) that present pathologic subdermal appearances of lymphoid infiltration without readily demonstrable hemopoietic changes. It is in these instances especially that the responsibility for diagnosis and treatment lies directly in the hands of the der-

*Read in Section on Dermatology and Syphilology, Southern Medical Association, Twenty-Ninth Annual Meeting, St. Louis, Missouri, November 19-22, 1935.

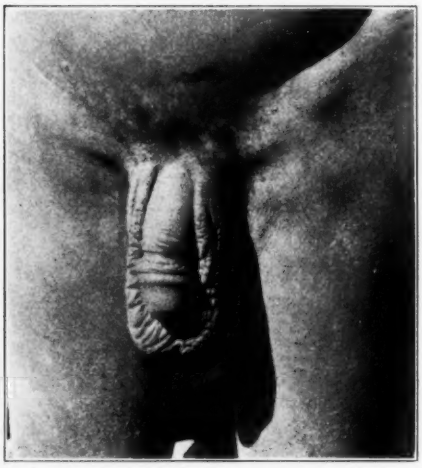

Fig. 1
Note enlarged lymph node.

matologist. Such cases have been discussed at length by Keim[2] and his associates. Sporadic reports of unidentified generalized dermatoses have appeared, in which it is apparent that the reporter seems somewhat undecided as to the nature of his patient's disease, but often for a lack of a more suitable diagnosis must label the condition "lymphoblastoma."[3] Experience has shown that some of these cases progress to a typical leukemia and result in death. Observations on some of the exfoliative types of lymphoblastoma have led many pathologists and dermatologists to the belief that in the beginning the disease is confined strictly to the skin, a lymphadenosis of the reticulo-endothelial system of the skin, and that the appearance of abnormal lymphocytes in the circulating blood is but a terminal manifestation.

The patient with a generalized exfoliative and edematous skin eruption presenting lymphoid enlargement and a typical derangement in his blood picture becomes at once classified as a leukemia with dermatologic manifestations. The prognosis is all too frequently considered fatal and he is given palliative treatment and doomed to die. But the patient with generalized erythrodermia, with intense intractable itching, who presents a slight lymphoid enlargement and a normal or nearly normal blood picture, is argued about pro and con while we wait for the lymphocytes to increase in his circulating blood. Too often examination of a pathological section of the skin or lymph node is postponed, and when it is done often the pathologists do not agree. This patient also receives only palliative treatment awaiting classification.

This fatalistic attitude and the postponement of treatment in these cases causes us to lose that golden opportunity of early and intense therapeusis which is so important in the cure of malignant disease. Often this opportunity is lost because the internist, the pathologist and the dermatologist will not or cannot agree, and neither will take the helm and steer a therapeutic course.

The following case report is illustrative:

A white American farmer, aged 45, first presented himself for treatment because of a violent itching eruption on the scrotum and upper legs. For a number of years he had had attacks similar in nature to the present attack about every six months, but had always cleared under simple remedies. The present attack had been unusually severe and was spreading on his legs.

His family and past history were irrelevant. He was a man of good habits, given to no special excesses and had always been generally healthy.

His first examination in the summer of 1933 revealed several well demarcated oval erythrematous and edematous scaling areas on the skin of the inner thighs. The scrotal skin was thick, swollen and scaly. He scratched at these areas during examination. The lymph nodes in the groin were slightly enlarged, firm and discrete, but not tender. A few weeks later these areas had spread, were weeping serum and the nodes in the groin appeared to be larger. A diagnosis of chronic neuro-dermatitis had been made, but he was referred to the hospital to rule out a possible lymphoid infiltration of the skin. The physical examination was essentially negative with the exception of his skin and the palpation of enlarged discrete, firm nodes in both inguinal regions and smaller similar nodes in the axillae.

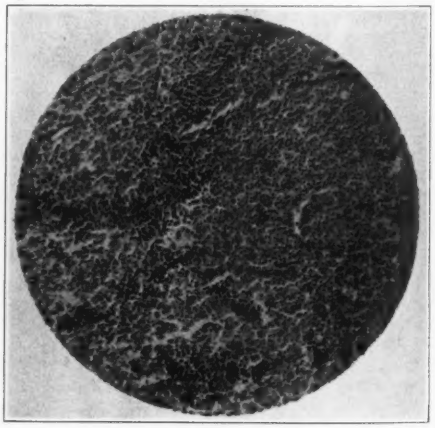

Fig. 2
Section of lymph node. Note tuberculoid arrangement of lymphocytes.

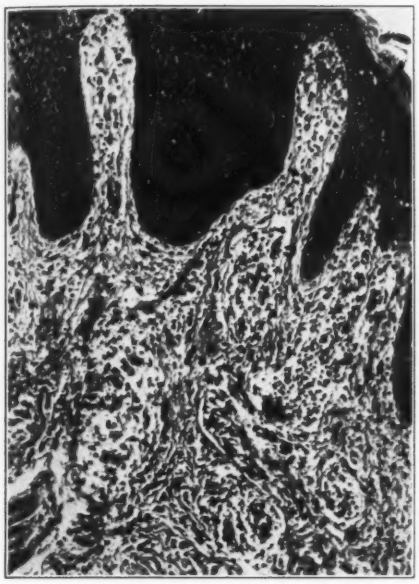

Fig. 3
Section of skin. Note infiltration with lymphocytes.

Pathologic examination of a section of the skin was not performed. On two occasions the blood count and blood picture were normal. The patient left the hospital unimproved and with no definite diagnosis. His erythematous eruption continued to spread and he was admitted to the United States Veterans' Hospital for observation. Examination October 24, 1933, revealed an increase in the size and extent of all his subcutaneous lymph nodes, loss in weight and an extension of his skin eruption with excessive pruritus and weeping and excessive thickening of his entire skin area. A clinical diagnosis of cutaneous lymphoblastoma was made in spite of repeatedly normal blood counts. X-radiation of his skin was advised and he was given three one-quarter units of unfiltered radiation at ten-day intervals with little or no improvement. Search for hematological evidence of leukemia was continued by the physicians at the hospital with no results, while his dermatological condition remained unimproved. Finally, after the failure of local applications, a portion of the skin and an inguinal lymph node were removed for pathologic examination.

The sections of the skin showed hyperkeratosis and parakeratosis with marked prolongation downward of the rete pegs. Throughout the corium extending to a great depth and especially in the papillae there was a diffuse lymphoid infiltration. This was composed mostly of lymphocytes with a generous sprinkling of eosinophils and neutrophils. The vessels were dilated. In some areas there was a suggestion of tuberculoid formation in the grouping of the cells, but no giant cells were seen. Sections of the lymph node showed a definite hyperplasia in the germinal centers with connective tissue proliferation. There was a tendency here as in the sections of the skin to a tuberculoid formation of the cells. Only a few eosinophils were present. Two pathologists examining these sections disagreed in their interpretations, the one considering the process inflammatory and the other lymphoblastoma of the skin.

The patient was sent to the Veterans' Hospital in Hines, Illinois, where a diagnosis of generalized erythroderma of the lymphoblastoma type was made after a thorough physical, x-ray and laboratory survey. While there he was fully hospitalized and at rest. From March 27, 1934, to June 6, 1934, he received unfiltered x-ray treatment in ¼ skin units (40 r units) and ¼ skin units (75 r units) doses to various portions of his body, receiving approximately an average of ¼ skin units (75 r units) each month, obviously too small a dose of radiation to be of any value to the patient. He was discharged and the prognosis was fatal.

On his return to Atlanta he was started on x-ray treatment in earnest in the hope that at least he could be made symptomatically more comfortable. At three-day intervals he was given ¼ unit (75 r units) of unfiltered x-radiation, alternating between his extremities and his body from June 17 to September 25. He thus received a total of 12 ¼ skin units (75 r units) to his entire body at intervals of a week. Improvement was slow, but definite, from the beginning. Fearing radiation sequelae, he was then given bi-weekly ultraviolet radiation for a six months period. During this time the itching and edema of the skin gradually disappeared and the palpable lymph nodes became smaller and more firm and today he is symptomatically and clinically well.

COMMENT

In the preceding case history we are aware that the pathological evidence, as ordinarily accepted, is insufficient for a clear-cut diagnosis of lymphoblastoma, but we feel that there is sufficient clinical evidence, when coupled with the pathological findings, to warrant a tentative prognosis of what might have occurred in the future if no intensive treatment had been instituted. We are also aware that the type of case described is given to remissions, only later to come to a typical leukemic death, and therefore the case is not reported as a cure. In the ready response to intensive x-radiation, ultraviolet therapy and rest it illustrates what may be accomplished by continuance of treatment in the face of a doubtful diagnosis. Unless this patient has a recurrence and develops a leukemia we may never be able to classify his condition definitely. But the important element is that today he is comfortable and apparently well.

We believe that in the beginning these cases are dermatologic problems and that the burden of the diagnosis and treatment lies directly in the hands of the dermatologists. We also believe that a biopsy and pathological examination of the tissue should always be done, but that a cut and dried pathological report should not be

wholly relied upon for the interpretation of the disease process.

As dermatologists we are prone to form habits of immediate clinical diagnoses which foretell a definite therapeutic approach, which in the majority of instances end in a cure or at least a solution of the problem. We too often hesitate to treat that which we cannot classify definitely, passing the buck to the internist, thence to the pathologist or the "clinical conference," until too many cooks spoil the broth, and we lose the golden opportunity for relief with early treatment. Such a series of events has occurred to us in experiences with several such patients as described above, and it has brought home to us the benefit that might be derived from an expression of our reflections and impressions on the management of this type of patient.

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THE GASTRITIS PROBLEM: NOTES ON HISTOLOGICALLY VERIFIED CASES*

By GEORGE B. EUSTERMAN, M.D.
Rochester, Minnesota

In the past decade there has been a marked revival of interest in gastritis. This is largely attributable to three primary factors: (1) the present vogue, especially on the continent of Europe, of performing gastric resection for benign gastric and duodenal lesions as well as for malignant lesions, thus permitting histopathologic study of fairly large portions of the freshly resected gastric tissue; (2) the more general use of the gastroscope, which has been greatly improved in recent years; (3) progress in the roentgenographic study of the mucosal relief. Accessory to these major factors are the following: accretions to knowledge from gastrophotographic observations; specialized studies of gastric function of the living; researches directed to the experimental production of the lesion; speculation as to the role gastritis plays in the genesis of ulcer, carcinoma, various forms of anemia, and postoperative sequelae; and finally, speculation as to the clinical significance of gastritis when associated with benign gastric and duodenal ulcer.

Although numerous problems are pressing for final solution with regard to this entity, the one of most concern to the physician and surgeon alike, in my judgment, simply stated, is this: to what extent is gastritis, or chronic gastroenteritis, the underlying cause in those conditions diagnosed as nervous indigestion, pseudoulcer, pseudocholecystitis, achylia gastrica, gastrogenic diarrhea, and so forth? Granting the necessity of a healthy skepticism, those who would disregard development in this field as of no particular significance should be reminded of two clinical facts: (1) in the past the physician has been content with looking on the stomach as being subject to only two diseases, ulcer and cancer. Although this is true in the larger sense, it is now known that other lesions, such as gastric syphilis, subdiaphragmatic hernia, pyloric hypertrophy of adults, chronic duodenitis, benign tumors, congenital deformities of various types, carcinoma masquerading as benign ulcer, and so forth, occur frequently enough to banish complacency; (2) reasoning from the standpoint of comparative pathology, as has Benedict, it is hard to deny the entity, gastritis, when physicians acknowledge, and repeatedly prove, the existence of such disorders as stomatitis, enteritis, duodenitis, hepatitis, colitis, proctitis, and so forth. Obviously solution of the problem is difficult because recognition of the lesion, whether circumscribed or diffuse, depends chiefly on the highly technical diagnostic procedure, gastroscopy. This procedure does not permit of application by members of the profession in general, but I feel that it is only a question of time when trustworthy information in this field will be crystallized and passed on to the general profession and that it will be applied in daily practice.

ETIOLOGY, PATHOLOGY, AND NOMENCLATURE

Faber stressed the importance of exogenous factors (chemical, mechanical, thermal, and bacterial) in the causation of acute gastritis and with his viewpoint most authorities are in accord.[8,9] He further held that chronic gastritis was usually the result of acute gastritis. On the other hand, Henning stated that knowledge of the cause of gastritis is entirely inadequate and that the cause was not determined in most of his cases. He recognized three general

*Read in Section on Gastroenterology, Southern Medical Association, Twenty-Ninth Annual Meeting, St. Louis, Missouri, November 19-22, 1935.

*From the Division of Medicine, The Mayo Clinic.

classes: the exogenous, the endogenous (eliminative, hepatogenous) and the types seen in association with various diseases. Buechner, as well as Hauser, ascribed to acid gastric secretion an important causative or contributory role in the so-called peptic gastritis. Konjetzny disputed Buechner's contentions, just as many authorities dispute the former's contention that gastritis and duodenitis precede the development of ulcer and cancer and predispose to these lesions.

From the standpoint of gross pathology, the surgeon should be suspicious of an inflammatory process in the stomach or duodenum in the presence of such external signs as edema, thickening of the antral portion of the stomach, congestion, increased vascularity, and perigastric adhesions. Such signs may exist singly or in combination. Gross and microscopic changes are usually more marked in the antral than in the fundic portion of the stomach. In the absence of external phenomena, macroscopic changes can be identified only by direct inspection of the mucosa after the stomach has been opened. This may reveal regional or diffuse ulcerations characterized by redness, edema, mucosal thickening, erosions, or ulcerations. The microscopic pathology has been well described by Konjetzny and his pupils, Simpson, Aschner and Grossman, and others. In the chronic variety, as the condition has been summarized by Gibbons, there are changes in the cells of the mucosa consisting of atrophy or "metaplasia" (goblet cells), that is, a reversion to the intestinal type; increased infiltration of the mucosa with round cells, and the presence of eosinophils; increase in size and number of the lymph follicles; increase in connective tissue of the mucosa; thickening of the submucosa, with round cell infiltration and increased vascularity. The mucosa may be thickened or thinned out (atrophic). Both the pathologist and the gastroscopist have pointed out the presence of edema and inflammatory exudate in the acute and subacute forms; also the presence of acute, subacute, and healed processes in the chronic forms in one and the same lesion, a condition which is attributable to persistent or renewed activity in inflammatory lesions of the mucous surfaces.

A glance at Table 1 discloses the involved nomenclature that has obtained, and that is attributable, in large measure, to the many-sidedness of the disease. Moreover, authorities in different countries have advanced their own classifications and terminology so that sub-types in particular might have various appellations; these in a measure are confusing to the average physician. It may eventually be the duty of some international scientific organization to outline and adopt a standard nomenclature satisfactory to all concerned, for the sake of clarity. One can even predict that the stage of the disease, its etiologic nature, anatomic situation, pathologic character, and the resulting functional derangement or complication may eventually be conveniently designated by a simple phrase such as the cardiologist employs when, for example, he says "chronic rheumatic mitral and aortic endocarditis with decompensation."

Table 1

THE NOMENCLATURE OF GASTRITIS

(1) Etiologic	(a) Exogenous (mechanical, chemical, thermal, bacterial) (b) Endogenous (eliminative, hepatogenous) and types seen in association with various diseases
(2) Anatomic	Corpus gastritis; antral gastritis
(3) Functional	Gastritis hyperacida, subacida, anacida, achylia absoluta, achylia perniciosa
(4) Gastroscopic	Hypertrophic, atrophic, catarrhal, hemorrhagic, erosive, ulcerative, polypous, granular, infiltrative, pseudomembranous
(5) Clinical picture and course	Acute, subacute, chronic, recurrens, dolorosa, larvata, progressiva, latens, exudans

SYMPTOMATOLOGY

From the symptomatic standpoint, the traditional conception of gastritis, of the chronic variety in particular, in contrast to the contemporary conception, is worthy of consideration. It is generally recognized that gastric disturbances engendered by gross gastric, duodenal or jejunal lesions are almost exclusively results of disturbed neuromuscular function which gives rise to disorders of motility, tonus and peristalsis, and to increased intragastric tension. Past teaching and experience led to the belief that changes confined to the gastric mucosa did not necessarily give rise to any frank gastric phenomena, with the exception of occasional hemorrhage and possibly of vague epigastric discomfort, although such indirect symptoms as anemia and intestinal disturbances, especially diarrhea, frequently occurred. The mucosal atrophy of pernicious anemia, or of sprue, pellagra, or idiopathic steatorrhea, whenever present, and that found in cases of uncomplicated atrophic syphilitic gastritis, usually give rise to little or no gastric disturbance. The same has been found to be true in cases in which the presence

of mucosal hypertrophy or hypertrophic gastritis have been confirmed by roentgenoscopic or postmortem examination. It seems difficult to reconcile this fact with the viewpoint of Faber, for example, that antral gastritis may give rise to symptoms closely simulating those of chronic pyloric or duodenal ulcer, or with the viewpoint of other observers, notably Henning, who has maintained that a variety of symptoms common to gross lesions of the stomach and duodenum may be engendered by the various forms of gastritis. Katsch, too, has described the following clinical varieties of gastric disorder, results of gastritis: (1) the "sensitive" stomach. By this Katsch had reference to "acidism" (epigastric burning, heart burn, eructation of acid material), easily provoked by dietetic error. (2) The pyloric syndrome. This closely simulates duodenal ulcer. The author, however, appropriately pointed out that in pronounced chronic cases of this kind an ulcer of the pyloric region or duodenum is usually found. (3) The third variety is divided into two subvarieties: (a) The weak stomach. In this condition the stomach is not equal to more than moderate demands, either qualitative or quantitative and not infrequently disorders of taste and appetite, and intestinal disturbances, are present. (b) Disturbances that are primarily intestinal. These are characterized by diarrhea, constipation, or gaseous distention. (4) Hyperchromic anemia (Faber's anemia) of patients who have achlorhydria. This condition reacts to treatment with massive doses of iron. (5) Gastric hemorrhage as the result of erosive gastritis in the absence of gross ulcer. This clinical picture has long been emphasized by Konjetzny, said Katsch. (6) A more acutely painful variety. This is the result of acute and subacute stages of gastritis.

In rare cases, Katsch also pointed out, the pains of gastritis may be so acute and intense, and accompanied by sufficient abdominal rigidity, that perforation may be suspected. In such cases satisfactory differential diagnosis may be impossible without surgical exploration.

Epigastric discomfort or pain in the presence of patchy or diffuse gastritis, in which the process is largely confined to the gastric mucosa, that is, in the presence of a superficial lesion, would presuppose associated spasm of the gastric musculature if the autonomic nervous system is irritable or unstable. Undoubtedly heightened sensitivity to pain also plays a part in some cases. Severe or neuralgic pains, such as make up the sixth clinical variety described by Katsch, have been attributed to inflammation of an infiltrative nature involving all the coats of the stomach and the process may include the nerve plexuses. Of course, in the presence of a stenosing pyloric lesion another obvious cause for pain and gastric disturbance is operative.

In the light of increasing experience it is obvious that gastritis in its various forms can give rise to the symptoms and signs noted by the authorities just cited. In my opinion, it is largely a question now as to how frequently gastritis is solely responsible for the symptoms; the circumspect practicing physician cannot escape the conviction at times that some pathologists, gastroscopists, even roentgenologists or other protagonists of gastritis as an important entity, are unduly imbued with an enthusiasm comparable to that displayed, on occasions, by some allergists and endocrinologists. One also gets the impression that the enthusiastic gastroscopist finds some abnormality of the gastric mucosa, to which undue significance may be attached, in the majority of cases in which he makes examination. Katsch himself has pointed out the fallacy of a diagnosis made exclusively from the results of gastroscopic examination in many instances because "a clear relation between gastroscopic findings and the clinical picture, even excluding everything but the subjective illness, can be established only in clear-cut cases with any degree of certainty." I have encountered several instances of patchy gastritis, histologically confirmed, in which operation had been performed erroneously for gastric ulcer or jejunal ulcer and in which I was by no means convinced that the gastritis was the cause of the symptoms. There are those who attribute to the associated gastritis, in cases of chronic gastric and duodenal ulcer, not only the cause of the symptoms, but the failure to effect cure by medical or surgical treatment. This is justifiable probably only in instances in which the gastritis is marked, judging from my experience. As previously has been stated, there are those who consider that gastritis is the precursor of all gastric ulcers and carcinomas, and that it is the cause of many, if not all of the sequelae of gastrojejunostomy or resection for gastric or duodenal ulcer. This again, in my judgment, is only partially justifiable and often is as difficult of proof as of denial. The need for further investigation and research in order to reconcile divergent or contradictory viewpoints is apparent.

CONCLUSIVELY ESTABLISHED CASES OF GASTRITIS

I herewith present a brief review of clinical types of gastritis which have come under my observation. The diagnoses have been confirmed at necropsy, by histologic examination of surgically excised or resected gastric tissue, or by combined clinical and gastroscopic, or by roentgenologic findings. The types are classified as follows:

(1) Acute gastritis: (a) exogenous, (b) corrosive, and (c) phlegmonous.

(2) Subacute gastritis: usually secondary to obstructing lesions of the stomach or duodenum, apparently both of mechanical and chemical, or of infectious origin.

(3) Chronic gastritis: (a) primary; (b) secondary.

From a histologic standpoint, as previously has been noted, distinct separation of the three types cannot always be made, because various degrees and stages of inflammatory changes are frequently found in the same specimen. The foregoing classification is based on the preponderant type of gastritis present.

Clinical and Pathologic Features.—The acute types have been discussed in detail elsewhere.[7] The ordinary exogenous type obviously is of frequent occurrence, usually is self-limited, and resolves with ordinary care. One recalls Beaumont's description of the gross appearance of the mucous membrane of St. Martin's stomach after the latter had been drinking "ardent spirits" for nearly a fortnight. According to Kaden, gastroscopic evidence of gastritis may persist for six to eight days after disappearance of all subjective discomfort. His observations, and those of others, have disclosed that increase in gastric secretory and motor function is characteristic of acute gastritis. Necropsy material at the Mayo Clinic contains specimens obtained in cases of acute hemorrhagic and necrotic gastritis following ingestion of poisonous bootleg liquor, lye, and other corrosives, as well as specimens obtained in seven cases of primary phlegmonous gastritis.

Simpson has pointed out that the use of the terms "acute," "subacute" and "chronic" are open to misinterpretation. Such terms, he has said, may in no sense imply length of clinical history or actual duration of the lesion. Many acute, erosive forms of the disease, for example, may remain acute and erosive for years; on the other hand, some cases appear to pass rapidly "from a condition of normality into the last stages of atrophy."

The subacute and chronic varieties, the familiar alcoholic variety, the syphilitic variety in its various forms, the atrophic variety associated with pernicious anemia, have been encountered clinically and at necropsy for years. Occasionally, and also over a period of years, the hypertrophic subacute and chronic forms have been seen in association with one of the following: hepatic disease, cardiac disease with decompensation, pulmonary tuberculosis, chronic cholecystic disease and certain metabolic, endocrine, and dermatologic diseases.

Of primary interest are those instances of gastritis encountered at operation and confirmed by histologic examination of excised or resected gastric tissue. Such cases can be classified conveniently in two main groups: (1) gastritis associated with other gross lesions of the stomach, duodenum, or jejunum; and (2) primary forms of gastritis. The first group is composed usually of cases of the subacute variety, in which the lesion is erosive, ulcerous, or hypertrophic; the lesions frequently are seen in association with pyloric obstruction attributable to duodenal ulcer or gastric carcinoma, less frequently in association with jejunal ulcer. Contributions to this phase of the subject, based on data supplied by surgical material, already have been made by Walters and Sebening and by Church, Walters and Wellbrock. *Figs. 1* and *2* are il-

Fig. 1

Resected specimen from a patient who had acute parenchymatous and ulcerous gastritis associated with duodenal ulcer.

Fig. 2

Section from specimen illustrated in Fig. 1. The following are noteworthy: exudate in the lumen; cellular infiltration and edema of the tunica propria. The specimen was taken high on the resected portion (x215).

lustrative of a case in which the duodenal ulcer did not give rise to pyloric obstruction.

Baker recently has made a critical histopathologic study of the gastric mucous membrane in a consecutive series of cases of carcinoma and of gastric and duodenal ulcer, irrespective of type, situation, extent, or whether or not any complicating factors were present. In practically all of the specimens of gastric carcinoma at least a small amount of pangastritis was found on microscopic examination; in 90 per cent of cases, the changes were atrophic in nature. Ninety per cent of the gastric ulcers were associated with some gastritic changes in the antral mucosa and 60 per cent of the total revealed definite atrophic changes. About 80 per cent of the duodenal ulcers were accompanied by some degree of antral gastritis, and in 30 per cent of these specimens the gastritis was of the atrophic variety.

Figs. 3, 4 and *5* are illustrative of the histologic changes observed by Baker in the mucous membrane remote from gastric cancer or gastric ulcer, even in the absence of pyloric obstruction.

Subacute forms of gastritis occasionally are associated with hypertrophy of the pylorus of adults; also they may be associated with subacute peri-anastomotic gastritis and with jejunal ulcer, especially in the presence of a malfunctioning stoma. Chronic types of gastritis occasionally are seen in association with chronic duodenitis. Subacute or chronic diffuse gastritis is the rule in association with benign and malignant polypoid lesions of the stomach. Many authorities are agreed that such polypoid lesions have their origin in gastritis, especially gastritis polyposa. Furthermore, some are of the opinion that because of the extensive gastritis or gastro-enteritis present the intrinsic hemopoietic factor of Castle is lost and a deficiency disease, pernicious anemia, ensues. The following report of a case is highly suggestive of this:

A man, aged 51 years, first came under my observation in May, 1924, complaining of a sore tongue, of eight months' duration, as well as of the fact that for a period of four weeks he had had frequent loose, watery bowel movements. The period during which he had passed watery stools had occurred about three months before his admission at the clinic. The man also had lost about 20 pounds (9 kg.) since the onset of his symptoms, and had lost somewhat in strength. His appetite was good and there was no paresthesia nor gastric disturbance of note.

Examination disclosed the presence of anemia (hemoglobin 66 per cent; erythrocytes 3,870,000 and leukocytes 12,100 per cubic millimeter of blood), glossitis,

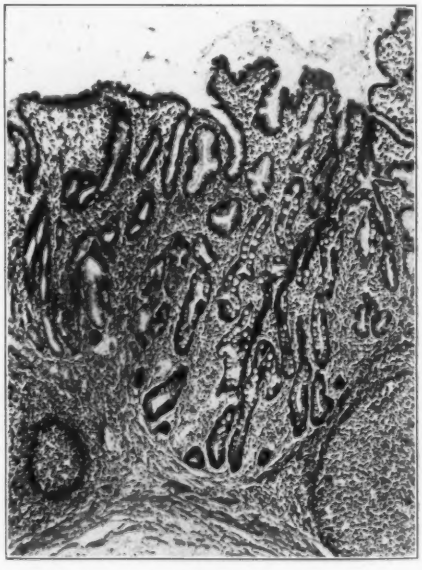

Fig. 3

Gastric mucosa containing collections of lymphocytes with secondary centers. The epithelium resembles that of the intestine. The case was one of gastric carcinoma (x55).

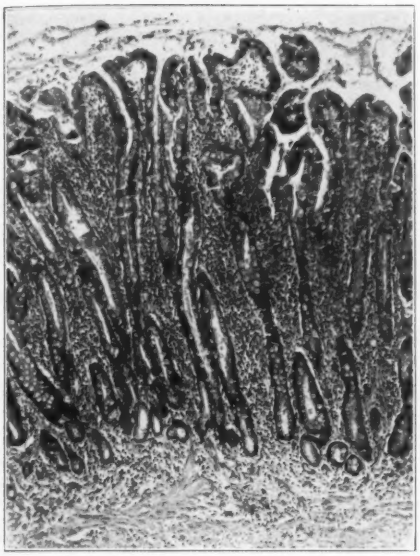

Fig. 4

Gastric mucosa with atrophy of parietal and chief cells. The epithelium resembles that of intestine with hyperplastic mucous cells. The case was one of gastric carcinoma (x50).

smooth tongue, and achlorhydria. A diagnosis of probable pernicious anemia was made, although neither at that time nor on subsequent examinations was there any definite evidence of subacute combined sclerosis.

The man was reexamined in October, 1924, because diarrhea had occurred and had endured for two weeks. There were no gastric disturbances. Examination at this time disclosed no abdominal masses or resistance, but the achlorhydria persisted. Owing to the presence of a few remnants of a meal eaten fourteen hours previously, roentgenologic examination of the stomach and duodenum was carried out and revealed an obstructive lesion at the pylorus.

In February, 1925, partial gastrectomy (Billroth I) was carried out and examination of the resected specimen disclosed early polyposis of the prepyloric gastric mucous membrane and regional gastritis. Undoubtedly, careful histologic examination of tissue remote from the pylorus would have revealed diffuse gastritic changes. This patient was under treatment before the days of liver therapy. Therefore transfusions of blood were repeatedly administered, sodium cacodylate was injected, and iron in massive doses as well as dilute hydrochloric acid were given orally. The same treatment had been given following the patient's first visit.

Reexamination, eleven months later, revealed a concentration of hemoglobin of 43 per cent; leukocytes numbered 4,600 and erythrocytes 2,010,000 per cubic millimeter of blood and the color index ranged from an original of 0.8+ to 1.0. There were also present moderate anisocytosis, poikilocytosis, and polychromatophilia. Occasional attacks of diarrhea persisted. Following the operation the man complained more of numbness of the hands than he had before.

The patient was seen in the clinic again in April and June, 1926, at which time he was much improved in every way and complained only of occasional glossitis and numbness in the hands. The value for hemoglobin was 49 per cent; erythrocytes numbered 2,750,000 and leukocytes 4,400 per cubic millimeter of blood. Transfusions were again ordered.

A report was received that the man had died January 16, 1927, at which time the attending physician had noted edema, hepatic enlargement, marked tachycardia and terminal coma. Necropsy was not performed, therefore the exact cause of death was never determined.

Speculation is rife as to the relationship of chronic gastritis with anacidity, to pernicious anemia and gastric carcinoma. Some authorities, notably Hurst, have contended that the basic factor is the atrophic gastritis which may result in either pernicious anemia or carcinoma. Hurst further has declared that with the methods of treating pernicious anemia, which are more effectual now than formerly, patients will live longer and gastric carcinoma eventually will develop. In the past hyperchromic macrocytic anemia, in association with benign or malignant tumors of the stomach and achlorhydria, has been regarded as a coincidence. The evidence for indisputable pernicious anemia in such instances was not always complete owing to the

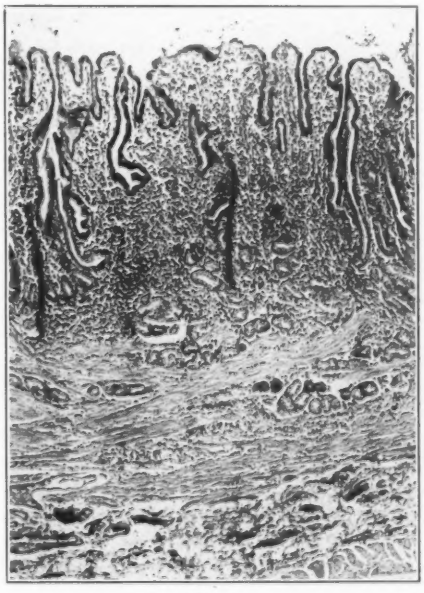

Fig. 5

Gastric mucosa with thickened muscularis which contains portions of glands. Many lymphocytes are in the tunica propria. Atrophy of parietal and chief cells is evident. The case was one of gastric ulcer (x60).

frequent absence of changes in the spinal cord, failure of the neutrophils to shift to the right, failure of the hematologist to find characteristic thinning and stranding of the individual lobes, and frequent absence of other hematologic and clinical features characteristic of pernicious anemia. When it is considered that in many cases of chronic gastritis with anacidity pernicious anemia never develops, or at most an "idiopathic," hypochromic anemia, and when it is recalled that an addisonian type of anemia fails to develop after total gastrectomy, Hurst's viewpoint cannot be unreservedly accepted until more careful and complete study of individual cases has been carried out. But accumulating evidence tends to support Hurst's contentions.

Primary Subacute and Chronic Gastritis.— Exclusive of organic gastric syphilis, which is always associated with extensive inflammatory, ulcerative or sclerotic changes of the gastric mucous membrane, the cases encountered at operation in the series which I surveyed were those in which the inflammatory process was sufficiently extensive to give rise to gross defects, usually antral in situation, and recognizable by the usual method of roentgenologic examination. Such defects were indistinguishable from those produced by carcinoma in particular, by syphilis, by chronic hypertrophy of the pylorus, or by gastric ulcer associated with antral spasm. They were usually considered to be caused by carcinoma. The question naturally arises as to how often gastric disturbances are attributable to patchy or diffuse inflammatory states unrecognized or misinterpreted in the absence of roentgenographic findings. One cannot help but feel that digestive disturbances of such origin are much more common than is generally believed, in the light of increasing experience, amply confirmed by gastroscopic examination or painstaking study of the mucosal relief.

In Table 2 are briefly summarized the salient clinical, pathologic and surgical features of some of the primary forms of chronic gastritis encountered at operation in the past ten years. In Cases 1, 2, 4, 7 and 10 there were filling de-

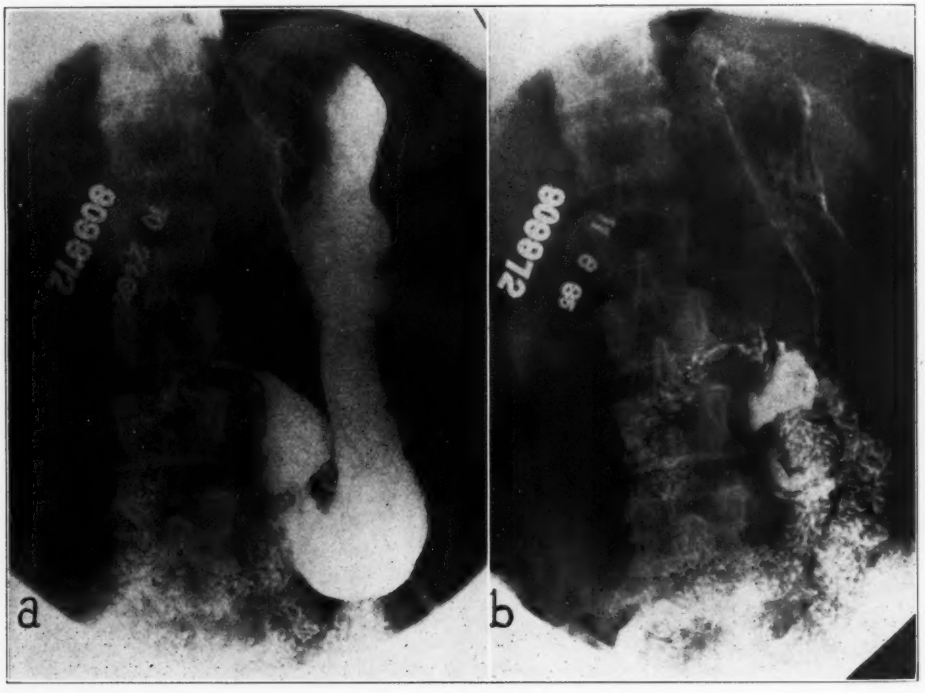

Fig. 6

(a) Multiple small superficial ulcers along the lesser curvature above the angle of the stomach. Roentgenoscopic examination disclosed effacement of the normal mucosal pattern. (b) Roentgenogram made two weeks later, showing the mucosal relief. The ulcers have disappeared or greatly diminished, but the internal relief is abnormally smooth.

Table 2

SUMMARY OF CASES OF SUBACUTE AND CHRONIC GASTRITIS IN WHICH OPERATION WAS PERFORMED

Case	Age and Sex	Major Symptoms and Signs	Roentgenologic Report	Clinical Diagnosis	Surgical Data	Pathologic Data	Remarks
1	58 F	Influenza two and a half years previously; since, progressive loss of weight and strength; anorexia, epigastric fullness and discomfort after small amounts of food; achlorhydria	Operable carcinoma of stomach	Gastric carcinoma	Partial gastrectomy	Chronic gastritis; extensive hyalinization of connective tissue	Improved
2	41 F	Intermittent brief attacks of "sour stomach," nausea and vomiting (seven years); loss of weight; gastric lavage gave relief. (No test meal)	Pyloric lesion with obstruction	Gastric tumor	Partial gastrectomy (Billroth I); cancer? ulcer? syphilis?	Chronic gastritis; multiple small adenomatous polyps	Reported cured eight years later
3	32 M	Acute epigastric pain, nausea, vomiting of very recent onset (six days); local physician suspected perforating lesion; marked anemia; achlorhydria. (Fractional analysis)	Perforated ulcer at pylorus	Perforated duodenal ulcer; pernicious anemia?	Diffuse antral thickening; partial gastrectomy (Billroth I) Nov. 1928	Chronic gastritis; moderate edema of walls. (No ulcer or carcinoma found)	Persistence of picture of pernicious anemia; gallbladder removed in 1933 with relief from painful seizures
4	42 M	For past eight months indigestion of progressive severity; anorexia, epigastric distress and fullness immediately after meals, lasting one to two hours; at intervals nocturnal nausea, fullness, emesis, loss of 15 pounds; aperients relieved; achlorhydria	Annular defect pyloric antrum; syphilis? cancer?	Cancer; syphilis of pylorus?	Obstructing mass at pylorus; partial gastrectomy	Chronic gastritis; plasma cell infiltration; spirochetes	Unimproved
5	32 F	Long-standing nervousness; vomiting spells usually when stomach empty; no pain; moderate loss of weight; heaviness in abdomen; achlorhydria	Lesion at outlet	Gastric ulcer	Area localized gastritis (3 cm. diameter) posterior wall near pylorus; excision mucosal specimen and posterior gastrectomy	Inflammation	Improved
6	36 M	For two and a half years intermittent attacks of epigastric pain two to four hours after meals, relieved by food and alkalis; worse for last three weeks, with emesis at night; pain followed by relief; lost 20 pounds in past five months; acids: 44 total, free 26; 180 c. c.	Gastric ulcer	Gastric ulcer	Area diffuse thickening and induration posterior wall of stomach, near incisura, partial gastrectomy	Edematous ulcerative gastritis (4 cm. diameter)	Two years later some epigastric fullness and sense of weight for one hour after meals
7	52 M	For ten years intermittent attacks of poorly localized abdominal distress appearing two to three hours after food, sometimes associated with nausea and vomiting; discomfort usually relieved by eating; total acids 28, free 10; 130 c. c.	Narrowing of pylorus and stomach. (Syphilis?)	Pyloric cancer?	Thickening and constriction of pyloric end of stomach; resection	Chronic gastritis; no evidence of ulcer or neoplasm	Three years later cured
8	58 F	One year prior to admission, painful attack upper right quadrant with extension posteriorly to right subscapular area; week ago severe localized pain in epigastrium, lasting one hour with nausea; total acids 40, free 26; 100 c. c.	Small pedunculated polyps pylorus and stomach	Gastric polyp	Marked thickening of pyloric end of stomach; no polyp found; resection	Specimen: 14 cm. stomach and 1 cm. duodenum; pylorus thickened, edematous and mildly inflamed	Reported herself as cured four years later
9	50 M	Typical duodenal ulcer-like symptoms for ten years; no bleeding, no loss of weight; total acids 60, free 44; 160 c. c.	Duodenal ulcer, small gastric ulcer	Gastric and duodenal ulcer	Diffuse and chronic gastritis; duodenitis; knife excision, cap, duodenum; gastroduodenostomy	Duodenitis	Temporary relief; hemorrhage three years postoperatively; gastroenterostomy and pyloric excision; fair health for seven years
10	58 M	For ten years ulcer-like complaint; chronic alcoholic; syphilis; gonorrhea, much medication; chronic nervous exhaustion; liver enlarged; negative Wassermann; total acids 92, free 80; 120 c. c.	Ulcerating lesions of pyloric end of stomach	Chronic gactric ulcer; carcinoma?	Cirrhosis of liver; pancreatitis; chronic marked diffuse hypertrophic gastritis; excision and gastroduodenostomy	Marked hypertrophic gastritis; chronic duodenitis (marked inflammation and fibrous mural thickening)	Much improved

fects of the pyloric antrum closely simulating the defect caused by carcinoma or syphilis, and in each instance the primary, or alternative, roentgenologic diagnosis was that of pyloric carcinoma. It naturally followed that this was the clinical diagnosis, in view of the obscure and comparatively infrequent nature of the lesion. One is inclined to agree with Konjetzny that those relatively infrequent forms of non-malignant, hypertrophic, stenosing pyloric lesions have their origin in, and are sequelae of, localized chronic antral gastritis, and it is not unlikely that some of my cases, reported as instances of hypertrophy of the pylorus of adults associated with antral gastritis, belonged in this category.

From a symptomatic standpoint the cases could be roughly divided into three types according to whether they simulated (1) cases of ulcer or of cancer with irregular symptomatology, (2) cases in which the symptoms closely simulated those of ulcer, or (3) cases characterized by pain or simulating biliary colic. Cases 1, 2, 4 and 5 could easily be classified as of the first type. Common to these four cases were pathologic changes confined almost exclusively to the pyloric portion of the antrum and having the appearance of scirrhous cancer on roentgenologic examination, achlorhydria, absence of pyloric obstruction and discomfort appearing soon after eating. Paradoxical as it may seem, the symptoms presented by this group may be similar to those of diffuse atrophic gastritis with anacidity. That gastritis may closely mimic chronic peptic ulcer is well illustrated by Cases 6, 7, 9 and 10, especially Cases 6 and 7, for in the last two cases the condition was associated with chronic duodenitis and this may have been the lesion chiefly responsible for the symptoms engendered. It is to be noted that free hydrochloric acid was present in the gastric content in all four cases.

Cases 3 and 8 were classified as of the third type. In Case 3 the pain may have been attributable to actual noncalculous cholecystitis, for the patient was greatly relieved after eventual removal of the gallbladder, in spite of the fact that preoperative cholecystographic studies, and examination of the organ by the surgeon when gastric resection was done, disclosed no gross external evidence of disease.

TREATMENT

The diagnosis and treatment of acute gastritis in its various forms have been discussed in detail elsewhere.[7] The acute and subacute varieties secondary to lesions of the stomach and duodenum, especially to obstructive lesions, require treatment of the original condition, chiefly surgical treatment. Konjetzny, in a personal communication, has recommended adequate preoperative treatment in cases of gastric and duodenal ulcer complicated by acute erosive gastritis or gastroduodenitis. Primary forms of subacute erosive or ulcerous gastritis, the diagnosis of which can be confirmed only by competent gastroscopic examination or occasionally by study of the mucosal relief, may respond to treatment such as that given for ulcer, and this treatment may be supplemented by gastric lavage with solution of silver nitrate made up in a strength of 5 to 20 grains (0.3 to 1.3 gm.) to the liter of water. *Fig. 6* illustrates the improvement in a case of subacute and chronic ulcerous gastritis after the first two weeks of treatment.

Treatment of chronic gastritis is often handicapped in those cases in which the causative agent is not determinable. When an exogenous factor, such as alcohol, tobacco, drugs, or strong tea or coffee is responsible, that factor must be avoided in the future. Imperfect mastication from rapid eating, missing dentures, or absence of molar teeth, should be corrected. The same is true of oral sepsis, the result of suppurative gingivitis or periapical abscess and of tonsillar infection. Infected sinuses should be drained and foci of infection elsewhere in the body (pelvic organs, prostate gland, anal region) should be removed if present.

Chronic gastritis, according to many observers, frequently is associated with pulmonary tuberculosis, chronic nephritis, hepatic cirrhosis, cholecystic disease, heart disease with decompensation, and certain metabolic, endocrine, and cutaneous diseases. In such cases the prognosis is dependent largely on the results of treatment directed against the major disorder, although treatment for gastritis, when the gastritis gives rise to symptoms, is also indicated.

From the standpoint of treatment directed to the stomach itself, all authorities are agreed that proper diet is of paramount importance. In principle, it should be bland and easily digestible, so that a minimum of motor and secretory activity will obtain. The smooth diet will prove useful, or the regimen for the treatment of ulcer will be found equally acceptable. Such treatment is especially indicated for gastritis of the erosive, ulcerative or hypertrophic type when associated with adequate secretion. The caloric

intake of patients who are overweight should be reduced, but the intake of cream, butter or olive oil, and of suitable carbohydrates, especially the latter, by those whose weight is less than normal, should be increased. Some physicians have found that fats and oils are not well tolerated in this condition. The dietetic measures just outlined may be indicated for three to six months or longer, depending on the rate of improvement.

There is some difference of opinion as to the nature and mode of administration of medicaments which should be employed. Naturally, these factors are also somewhat conditioned by the type of gastritis that is being treated. The treatment for the erosive, ulcerative, or hypertrophic type has already been discussed. For the type characterized by anacidity, or for the atrophic type, Hurst has recommended lavage with a pint (500 c. c.) of warm water to which 1 fluid ounce (30 c. c.) of hydrogen peroxide has been added. In this way it is claimed that mucus can be effectively removed, and frequently free acid is again noted in the gastric content. Treatment in cases of diffuse atrophy of the mucosa is invariably useless. However, 45 to 60 drops of dilute hydrochloric acid taken in milk or orangeade with meals frequently is indicated, especially in the presence of diarrhea. Enzymes, such as pepsin and diastase, are regarded as ineffectual by most authorities, but they may be tried. An alkaline powder containing about 20 grains (1.3 gm.) of bismuth subcarbonate and 10 grains (0.65 gm.) each of heavy magnesium oxide and sodium bicarbonate, taken one or two hours after meals, in water, is useful, even in the absence of excess free hydrochloric acid in the gastric content, to relieve heart burn, epigastric distress, and constipation. In cases in which there is anacidity or subacidity, the use of orangeade, tomato juice, and vitamin A concentrates may be indicated. In cases associated with marked anemia, liver extract or stomach mucosa usually is indicated. Jones, Benedict and Hampton have shown the striking improvement in the appearance of the gastric mucous membrane following successful treatment of pernicious anemia. Polypoid lesions, chronic antral lesions giving rise to defects indistinguishable from carcinoma such as are illustrated in Table 2, and chronic lesions presumably of gastric nature giving rise to recurrent hemorrhage, usually require surgical treatment.

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CHRONIC INFECTIOUS ATROPHIC PROLIFERATIVE RHEUMATOID ARTHRITIS*

By JULIAN E. GAMMON, M.D.
Jacksonville, Florida

In 1932 I reclassified arthritis into five major groups from an etiological point of view.† These five distinctive groups are: (1) the infectious, (2) the metabolic, (3) the allergic, (4) the traumatic, and (5) the neuropathic. Each group is represented by a distinctive type of arthritis, but frequently there is more or less overlapping of one or more of these etiological factors. In 1933 the heads of the arthritic clinics at a meeting in New York adopted a similar classification.

It is quite clear that arthritis due to infection may be divided into two groups: one due to infection within the joint and classified ac-

*Read in Section on Gastroenterology, Southern Medical Association, Twenty-Ninth Annual Meeting, St. Louis, Missouri, November 19-22, 1935.

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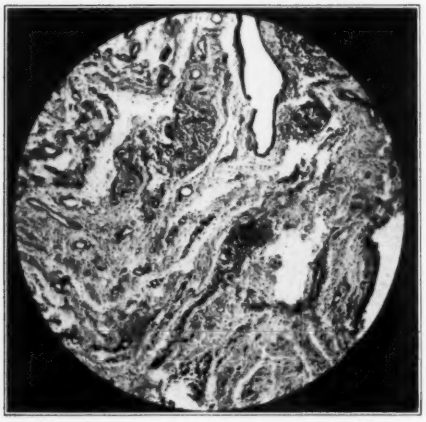

Fig. 1
Thickened synovial membrane with marked increase in blood vessels, fibrous tissue, lymphoid tissue. Bacteriologic cultures sterile.

cording to the infection, the other due to infection elsewhere in the body. Arthritis of focal origin with a sterile joint has been the source of much speculation and comment, and has been classified under several headings. The full given name is chronic infectious atrophic proliferative rheumatoid arthritis.

Now, let us consider the pathology. The inflammatory reaction in the joint may involve the peri-articular structures, the synovial membrane, and the subchondral bone, the epiphysis. And as the disease progresses the joint cartilage is destroyed, the joint develops loose motion and subluxation may take place. The joint capsule is markedly thickened and usually distended with fluid. A panus of granulation tissue extends from the synovial membrane across the joint surfaces, gradually destroying the cartilage. There is a similar granulation tissue reaction in the connective tissue of the marrow in the subchondral bone which honeycombs the cartilage from beneath. In the less rapid destruction of the joint there may be proliferation of the endosteum of the epiphysis and ankylosis may occur.

I should like to show some lantern slides made from the thickened synovial membrane and the pannus of granulation tissue, the cultures of which were sterile. *Fig. 1* shows a marked increase in the blood vessels and fibrous tissue. *Fig. 2* shows a marked increase in the lymphoid tissue and definite lymph follicles; *Fig. 3*, branching of the villi. At operation upon this patient, granulations could be seen honeycombing the cartilage from beneath and this explains why synovectomy frequently fails to restore the joint to normal function.

I have a lantern slide of an x-ray film indicating destruction of the joint and subluxation, and a slide of an ankylosed spine occurring at the age of twenty-five after ups and downs from an arthritis beginning at the age of

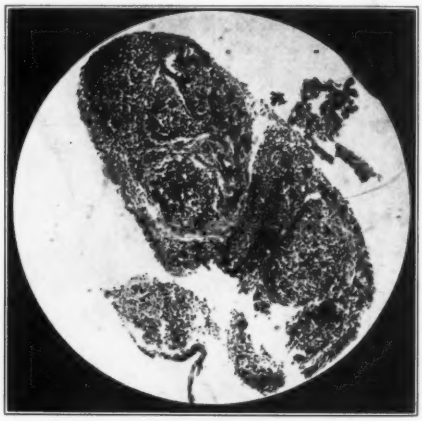

Fig. 2
Terminal portion of villus composed almost entirely of lymphoid tissue. Bacteriologic cultures sterile.

Fig. 3
Branching of the villi. Bacteriologic cultures sterile.

18. The focus of infection, in the latter, is a chronic suppurative prostatitis from which a pure culture of *Staphylococcus albus* was grown, and the intradermal test was strongly positive to the staphylococcus vaccine. The x-ray films indicate obliteration of the intervertebral articulations and a bony fixation in the cervical portion. There is diminution of the intervertebral spaces and a marked fusion of the borders of the vertebrae by dense bony spurs in the dorsal and lumbar regions. This arthritic process, at first glance, may be confused with hypertrophic or osteo-arthritis.

The usual pathogenic bacteria found in foci of infection are: *Streptococcus hemolyticus, non-hemolyticus, viridans, Staphylococcus albus* and the gonococcus. The foci of infection may be divided into two groups, the first group accessible to complete or partial surgical removal and culture, and the other group more or less inaccessible to removal and bacteriological culture. Here in lies the problem of therapeutics. Dental apical infection can be completely removed and our therapeutic results are far better than the attempted removal of any other focus. We must keep in mind the fact that the organisms cultured from the foci are the types which do not produce permanent or lasting immunity. This necessitates vaccine therapy, which can be carried on sufficiently long to rid the body of the organisms which were not removed when the focus was removed.

What is the value of vaccine therapy? This question has been discussed pro and con for many years and no agreement has as yet been reached. In studying this question I have chosen the prostate as an accessible organ upon which to study the effects of vaccine therapy and its relationship to arthritis of gonococcus origin. I selected a patient with a gonorrheal prostatitis. The gonococcus had been identified in the pus massaged from the prostate, and the arthritis had totally disabled him. I first had a competent genito-urinary specialist clear the prostate of pus and I began injecting intradermally in graduated doses gonococcus vaccine, and I observed four distinct reactions: first, a local sensitive reaction in the skin; second, a marked increase of pus from the prostate; third, a temporary increase of stiffness and soreness in the joints; and fourth, a general systemic reaction with fever 102°. The vaccine was discontinued and local prostatic treatment was again done, and the prostate was again cleared of pus. The patient's arthritis, which had kept him on crutches, was much improved and he was anxious to have the vaccine therapy continued. After a second course of vaccine the same reactions occurred. The prostate was heavily loaded with pus and local prostatic treatments soon cleared the pus which contained no demonstrable gonococci. The patient's arthritis was nearly well. A third course of vaccine was given and a similar reaction occurred in the prostate. For the fourth time the prostate was cleared of pus, which contained no organisms, and the patient was free of his arthritis and has been well for more than a year.

I have had a similar experience with *Staphylococcus albus* focal infection in the prostate, but the vaccine must be more concentrated.

I have not had the opportunity of studying streptococcus focal infection in the prostate, but elsewhere streptococcus vaccine for treatment of focal infection should be about half the concentration of the staphylococcus. Strains of streptococci are, however, the most frequent organisms found in foci of infection, particularly about the head.

In conclusion, I want to state that our best results in treating arthritis of focal origin are obtained early and before extensive damage is done to the joint. Dental apical focal infection can be more completely removed than any other focus and our therapeutic results are striking and far better than the attempted removal of any other focus of infection. Cultures should be made from each focus when its removal is attempted. Vaccines are of value when judiciously used in activating the defensive mechanism against the specific organisms in the primary and secondary foci. Vaccines are of little value in desensitizing the joint; in fact, the joint symptoms are frequently more marked for a day or two after vaccine injections intradermally. Vaccines are of no value in the treatment of acute infectious diseases where the defensive mechanism is already stimulated to the utmost. And finally, may I add, there is no drug or diet which will cure arthritis of focal origin, however, blood transfusion may be lifesaving.

GASTRO-INTESTINAL SYMPTOMS OF KIDNEY DISEASE*

By WALTER E. VEST, A.B., M.D., F.A.C.P.
Huntington, West Virginia

Broad indeed is the twilight zone between pure gastro-enterology on the one hand and internal medicine on the other, and there is such an overlapping of clinical pictures in the abdomen that one scarcely knows where internal medicine ends and gastro-enterology begins. Recently I saw the term gastro-enterologist defined as "a specialist in gastro-enterological examinations clarifying his special subject, but primarily an internist versed in problems of internal medicine."

The digestive tract is very responsive to stimuli in other parts of the body, being a mirror, if we may use such a simile, in which is reflected departures from well-being elsewhere in the organism. Considering these fundamental facts, it behooves us then to measure up to the definition just quoted and be good internists first and good gastro-enterologists afterwards. With the thought in mind that not enough attention has been paid to digestive symptoms dependent upon pathologic conditions outside the alimentary tract, my subject today was chosen. In very recent years the relationship between renal cause and digestive effect has been studied by various authors, notably Brown, Smith, Colby and Abeshouse. The article appearing in the October issue of *The American Journal of Digestive Diseases and Nutrition* from the pen of Abeshouse is very comprehensive. It includes the entire upper urinary tract and has been especially valuable to me.

Indigestion as a symptom of renal disease was first impressed upon me some nineteen years ago when a middle-aged man consulted me because of a chronic indigestion and prefaced our interview with the comment that no medicine was any good for indigestion, because in the preceding eleven years he had taken some out of every bottle in the Guyan Valley without any relief whatsoever. His symptoms were those of a chronic gastroduodenal ailment, but careful examination showed no disease in the alimentary tract. His urine, however, contained considerable pus and the scout plate showed a large stone in the right kidney. I introduced to him my confrere, who wielded the scalpel with the assurance that surgical removal of the renal stone would cure his indigestion. The old fellow cogitated a minute or two and then replied: "I guess I'd better go back home and get right with God before I let you boys whack on me." It must have taken him some time to "get right" because he did not return for over three years, by which time he had a pyonephrosis with complete destruction of the kidney, requiring nephrectomy and a long and stormy convalescence.

Just why should pathologic renal conditions give digestive symptoms? Apparently there are three basic causes: (1) the nerve supply by means of which there is a reflection of symptoms from the kidney to the digestive tract; (2) the close anatomical relationship of the right kidney to the stomach, duodenum, gallbladder, pancreas and the ascending and transverse segments of the colon; and (3) the blood stream element or, as Brown terms it, "the circulatory factor," which may be purely physical, as stasis, but is much more often toxic in nature due to circulation in the blood stream of the products of infection, either acute or chronic; or the retention therein of toxic material resulting from either impaired metabolism or poor elimination, or both. The proximity factor is enhanced by the fact that the localizing mechanism of the organs in question is rather indefinite.

The chief underlying cause, certainly from the numerical standpoint, is the interrelated nervous mechanism of the kidney and the digestive tract, the nervous "hook-up," if we may borrow a term from the world of radio. Smith has shown that the renal nerve supply is derived from the cerebrospinal system by means of the sixth to twelfth dorsal and the first and second lumbar nerves which send fibers to the celiac ganglion and through this to the renal plexus, from which the kidney is directly supplied. The parasympathetic vagus sends excitomotor fibers to the celiac plexus, thus communicating with the renal plexus, which receives fibers also from the splanchnics, the inferior mesenteric ganglion and the first lumbar sympathetic ganglion. The digestive tract from the stomach through the transverse colon is supplied by the vagus, by the white rami from the fifth to twelfth thoracic nerves, and by the inhibitomotor sympathetic, largely through the celiac ganglion. Impulses from the kidney, after reaching the cord, pass upward and by means of the tractus solitarius to the nucleus of the vagus, from which they are reflected to the stomach and intestinal segment, receiving a vagus supply, resulting first in diminution of gastric and intestinal motility and later in an increase. When the stimulus is reflected over the sympathetic fibers, there is inhibition of peristalsis and constipation results. Earlam and Brown have demonstrated that the renal capsule has a specific nerve supply of its

*Chairman's Address, Section on Gastroenterology, Southern Medical Association, Twenty-Ninth Annual Meeting, St. Louis, Missouri, November 19-22, 1935.

own derived entirely from the renal plexus and that by means of this capsular innervation the sensation of localized renal pain is received when the pelvis is distended by ureteral block with consequent hydronephrosis. Stimuli of the renodigestive reflex may be either: (1) by irritation of the mucous membrane pelvic lining by a stone, bacteria, pus or blood clot; (2) by block of the pelvis which distends the capsule and gives rise to fairly well localized pain as well; (3) by inflammation or new growth in the parenchyma; (4) by the pull exerted by a movable kidney and (5) by irritation of the posterior layer of the peritoneum reflected over the kidney. The symptoms resulting from these different stimuli vary in different individuals and from time to time in the same person. The stoic who responds sluggishly to almost any stimulus may have from a renal stone a very different sensation from that experienced by a labile neurotic individual. Since the response to reflected stimuli may be either sensory, motor or secretory, it is not surprising that the symptomatology is varied. The patient's usual complaints, which he attributes to "indigestion," are: abdominal discomfort, often amounting to real pain; nausea, and, at times, vomiting; gaseous distention, eructation of sour material, constipation, and now and then diarrhea. These are often grouped to mimic a peptic ulcer or cholecystic disease. Cases in the latter group have been reported showing jaundice, a symptom due to traction upon the duodenum and bile ducts sufficient to produce a blocking of the common duct. In children especially the differential diagnosis between acute pyelitis and acute appendicitis may often be extremely difficult. Acute nephritis, or an acute exacerbation of a chronic parenchymatous nephritis, may simulate very closely an acute surgical emergency in the abdomen. Diarrhea is most often toxic. The gaseous distention is usually sympathetic in origin and is especially noticeable after operations upon the kidney.

The following case report is an instance in which all the symptoms pointed to the digestive tract and the pathologic condition was entirely urinary:

A white locomotive engineer, age 40, was admitted to the hospital November 19, 1933, complaining of upper abdominal pain and vomiting. About six years previously he had had a similar but milder attack with dull aching abdominal pain and occasional vomiting. After about four weeks the symptoms disappeared and he felt well again. Since then each autumn he had had similar attacks lasting from two to four weeks, after which he felt practically as well as usual. About the middle of August preceding admission, such an attack had come on and instead of clearing up had become steadily worse. Upon admission he had a constant upper abdominal pain, most marked on the left. At times there were sudden severe pains in the left upper quadrant. These did not radiate and lasted only a moment or two. He complained of sour stomach and the eructation of much gas. For a month he had vomited daily, and vomiting had been followed by temporary relief. When the pain became very severe, he induced vomiting for the relief which it afforded. Blood had never been present in the vomitus and the stools had never been tarry. The appetite had remained good, but he had been afraid to eat freely, especially heavy foods, and had lost considerably in weight. The taking of food had no immediate effect on his pain, however. For some weeks he had been unable to sleep well, owing to the pain and nausea. He had noticed that with each attack he had been constipated, but when the other symptoms disappeared the bowel movements were regular. There had been no urinary symptoms of any nature, and there was nothing noteworthy in either the past or the family history.

The physical examination showed a sallowness amounting to a questionable jaundice, much dental sepsis, and moderate tenderness over the left upper quadrant. The liver and spleen were not enlarged and the gallbladder was not palpable. Masses could not be made out, although there was a definite sense of resistance over the entire upper abdomen. The temperature, pulse and respirations were normal.

The urine, which was acid, showed a trace of albumin and many pus cells. The red blood cells numbered 4,550,000 and the white 11,250. The polymorphonuclear count was 78 per cent, lymphocytes 20 per cent, transitionals and eosinophils each 1 per cent. The hemoglobin was 85 per cent Dare. The blood sugar was 129 mgs. per 100 c.c. and the nonprotein nitrogen 44. The Wassermann and Kahn reactions were negative. The icteric index was recorded as less than 15. The fasting gastric contents showed a volume of 45 c.c., free hydrochloric acid of 26 degrees and a total acidity of 49. The corresponding Ewald values at the end of an hour were: volume 195 c.c., free hydrochloric acid 29, total acidity 48. The benzidine reaction was negative in each specimen.

The cystoscopic examination done by Dr. R. M. Bobbitt disclosed a normally functioning right kidney. The left kidney, however, showed a calculous pyonephrosis and was functionless. Roentgen examination of the gallbladder and gastro-intestinal tract disclosed no organic pathologic condition in either system.

Left nephrectomy was done by Dr. Bobbitt on December 4, 1933. One large stone was found in the pelvis and a small one in the ureter.

The digestive symptoms gradually subsided and after eleven days disappeared entirely. He was discharged December 28 and has had no digestive symptoms since.

A phase of renodigestive symptomatology which has not been stressed in the recent literature is the mimicry of the acute surgical abdomen by acute nephritis, or by acute exacerbations of chronic nephritis. We were able to find only very slight reference to such a syndrome and no case report. Within the past decade the author has seen three such cases of which the following is illustrative:

On September 27, 1935, about 11 a.m. a white male, age 60, who had been known to be for several years a hypertensive renal vascular victim, began to have fairly marked abdominal pain which was most severe on the right but was fairly well generalized. He was nauseated but did not vomit. The pain was fairly constant for the remainder of that day and during the night. There was some distension from the onset and this symptom gradually increased. At 2 a.m. on September 28 the patient, who was himself a physician, after telephoning a confrere had a nurse give him a hypodermic of morphine, which gave him considerable relief, but did not entirely ease the pain. There were no urinary symptoms except a moderate decrease in volume output. The nausea continued and about 9 a.m. he was seen by a fellow physician who found the temperature 100°, fairly marked abdominal pain, moderate distension, and considerable rigidity. Inasmuch as the patient felt himself improved, hospitalization was not insisted upon. By noon the nausea was gone and the pain definitely lessened. At 1 p. m., of his own volition he took an ounce and a half of castor oil and shortly thereafter the nausea returned and the pain gradually became worse. At 4 p.m. he vomited, the ejected material being largely the oil taken three hours earlier. Several enemas were given him during the day, none of which was very effectual, although some fecal matter had been discharged, and considerable relief had been experienced for about thirty minutes after each enema. While never entirely free from pain, he was fairly comfortable until about 2 a.m. on September 29, when the pain became distinctly more severe. I saw him in consultation about an hour later and found his temperature 100°, pulse 88, abdomen considerably distended, tender on pressure and fairly rigid, especially on the right. Nausea was still present. He was sent to the hospital and upon admission the temperature was noted as 100.6° and pulse 84. The urine showed heavy albumin, specific gravity of 1,031, a considerable number of pus cells and a few erythrocytes. There was an average of ten granular casts per high power field. On September 19, that is ten days previously, his urine had been analyzed and found to have a specific gravity of 1,022, a trace of albumin, and approximately 20 pus cells per high power field. An occasional granular cast had been noted. Upon admission to the hospital, the blood count showed red cells 4,190,000, hemoglobin 72 per cent, white cells 24,200, polymorphonuclears 88 per cent, lymphocytes 9 per cent, monocytes 3 per cent. The nonprotein nitrogen was 58 mgs. per 100 c.c. Ten days earlier the count had been red cells 4,050,000, white cells 9,500, hemoglobin 75 per cent, polymorphonuclears 75 per cent, lymphocytes 33 per cent, monocytes 3 per cent and eosinophils 1.

Surgical consultation was obtained and it was agreed that the abdomen should be explored because of the nausea, the fact that the distension and rigidity appeared to be increasing, and the pain was unimproved and very annoying. Laparotomy was done at 10 a.m., and except for moderate gaseous distension of the gut, the entire contents of the abdomen were normal. The temperature went to 101° the day after operation but was never so high again. By the fifth day the urinary picture was approximately what it had been ten days before the acute exacerbation, and it has remained practically the same since. No unusual postoperative pain or distension was noted and convalescence was otherwise uneventful. He was discharged October 11.

This case demonstrates well the difficulty one at times experiences in differentiating an acute exacerbation of a chronic nephritis from surgical abdominal conditions.

SUMMARY

Very frequently the presenting symptoms of renal disease are referred to the digestive tract, and almost any gastro-intestinal syndrome may be mimicked. This phenomenon may be (a) toxic; (b) physical; or (c) nervous in origin. By far the great majority of such instances are due to the nervous mechanism, the stimulomotor symptoms being reflected to those parts of the alimentary tract which are supplied by the vagus and the depressomotor stimuli being reflected over the sympathetic fibres. Attention is directed to the fact that occasionally an acute nephritis, or an acute exacerbation of a chronic nephritis, may simulate very closely acute surgical abdominal disease.

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DIET AND SURGERY IN THE CURE OF GASTRIC AND DUODENAL ULCERS*

By EARLE DRENNEN, M.D.
Birmingham, Alabama

The management of gastric and duodenal ulcers continues to be a problem of vital interest to physicians and surgeons working in this field. In the first place, let me say that I do not presume to offer suggestions as to diet or the medical treatment of these conditions.

The few facts that I shall try to present to you, come from the analysis of 100 cases of duodenal and gastric ulcers, upon which I have operated. Sufficient time has elapsed in practically all of these cases to permit of definite opinions as to the end results. A few of the earlier cases in this small series were operated upon as long as 20 years ago.

There is no question today that peptic ulcer is primarily a medical and not a surgical condition. The ideal time for medical cure is when the ulcer and patient are both young Gastric surgery does not give satisfactory results in young people and should not be instituted except in emergencies.

As to the etiology of peptic ulcer, it seems generally agreed that a localized area of lessened resistance permits the gastric juice to digest the mucosa, and thus an ulcer begins. The exciting causes may be grouped under three headings.

(1) *Hyperacidity.*—In this condition Dragstedt has recently shown experimentally that a pure gastric juice containing about 135 clinical units will cause ulceration in any part of the gastro-intestinal canal when more or less constantly applied.

(2) *Toxins.*—Burns and certain strains of streptococci are examples.

(3) *Neurogenic.*—Cushing noticed superficial peptic ulcers after certain brain operations and pointed out a great increase in duodenal ulcer during the most painful part of our financial depression.

A predisposing cause, which is most important, is the tendency toward ulcer, which certain individuals inherit. A certain type of individual which has come to be recognized, often shows marked tendency to ulceration and recurrent ulceration.

Two habits which contribute most to the formation of peptic ulcers are smoking of tobacco and the drinking of alcohol. The excessive, long-continued inhalation of cigarette smoke can mimic perfectly all the symptoms of ulcer. It is even possible that the sympathetic ganglia are poisoned by nicotine and pyridine, causing vascular disturbance. It is known that vascular disturbance in the peripheral vessels of the lower extremities is caused by long continued smoking. Seventy-five per cent of our patients smoked excessively and inhaled the smoke. There can be little doubt that smoking becomes a mild drug addiction. Three of our patients are perfectly well when abstaining, but prefer smoking with slight digestive disturbances. A perforated duodenal ulcer patient, while recovering, once told the author that he would gladly repeat the experience of perforation and operation, rather than give up smoking.

It has been my observation that the physician who smokes to excess usually tells his patients that smoking does no harm. It may not be beyond the bounds of reason to hope that some day, we shall cure pyloric spasm and ulcer by attacking the sympathetic ganglia and nerves which preside over the upper abdomen.

As we commonly learn more from our failures than from our successes, it may not be amiss to consider what constitutes a failure in the treatment of these conditions. The failures of medical treatment may be summarized as:

(1) Pain and indigestion, which are disabling, the patient being unable to follow his occupation.

(2) Severe hemorrhages.

(3) Perforation.

(4) Obstruction.

(5) Malignant changes.

However, as a rule, the failures of medical treatment are far less serious than those of surgery. The triumphs of gastric surgery may be greater than those of medical treatment, but the failures of surgery in this field are among the most distressing known. Patients with gastrocolic fistulae are the most pitiful creatures imaginable, many of them condemned to death by the only procedure which offers hope of cure.

It is to the credit of medical treatment that it rarely leaves the ulcer patient in a worse condition, but the same cannot be said of surgery. A few concrete cases of surgical failure may be worth recording.

Case 1.—In 1927, we operated upon a woman, aged 43, for duodenal ulcer. She had undergone long and

*Read in Section on Gastroenterology, Southern Medical Association, Twenty-Ninth Annual Meeting, St. Louis, Missouri, November 19-22, 1935.

competent medical treatment, without relief. At operation the ulcer was excised and a pyloroplasty done. She was well for a year. At the end of this time the ulcer had recurred; and, at the second operation, although the duodenum was widely open, and the stomach emptied quickly, the free hydrochloric acid being 22 and total 28, a posterior gastro-enterostomy was done. She was well for four years, then fairly well for two years. Six years after the gastro-enterostomy, a definite jejunal ulcer was present. This was removed during the past year. Her condition was too bad to permit of partial gastrectomy, which she still needs. In this case the gastro-enterostomy was a failure of surgical judgment. A resection of the stomach, taking away about three-fourths of the organ, would probably have cured her completely.

Case 2.—Twelve years ago an Italian merchant with duodenal ulcer and marked pyloric obstruction was referred by Dr. H. P. Shugerman. The stomach showed fairly high acidity. A posterior gastro-enterostomy was done. He soon regained his health, added 40 pounds to his weight, and remained well for eleven years. At the end of this time he began to have a painful indigestion and occasional severe hemorrhages. At operation a few months ago a large bleeding jejunal ulcer was found. The pylorus was almost completely blocked. We wished to resect the stomach, but his condition would not permit, so the anastomosis was taken down and a gastro-duodenostomy was done. He is doing well, but still has hyperacidity. This case showed a good result for eleven years, then a failure. This shows the longer one observes his cases the poorer his statistics become.

Case 3.—A man 48 years of age had had a gastro-enterostomy done elsewhere three years previously. He was referred by Dr. Seale Harris. The patient had a jejunal ulcer with a chronic perforation, which permitted the jejunum to communicate with a small abscess cavity, whose walls were formed by the parietes and one side of the mesentery of the jejunum. He was intolerably miserable. At operation, it was necessary to resect the stomach and a small part of the jejunum. The patient did well at first, then began a septic fever, and death occurred in five weeks. Autopsy showed hundreds of small abscesses throughout both lungs. In this case, to do nothing would have been inhuman; and, although the patient died, the failure was one which left no sting.

Case 4.—A physician 43 years of age had been operated upon 17 years before for perforating duodenal ulcer. He continued all his life to have digestive disturbances and occasional hemorrhages. He had severe hemorrhages in 1926 and again in 1928, necessitating transfusions. He did not vomit blood, but could taste it. There was much blood in the stools. In 1930 there were more hemorrhages. In 1933 they became so severe as to require five transfusions in two days. He was 5 feet 6 inches high and weighed over 200 pounds. In July, 1933, a partial resection of his stomach was done, about one-third being taken away. After a year he again began to bleed, not so severely as formerly, but more persistently. Again he demanded operative relief. A large jejunal ulcer was found. Resection of the affected portion of the jejunum was done and competent resection of the stomach with resection of the duodenal ulcer. He took the anesthetic very badly. Two transfusions were given. He died four days later in uremia, having passed no urine since the operation. Here a bold resection at the first operation, or spinal anesthesia at the second, might have saved him.

Case 5.—A man, aged 45, who stated that he did not care to live, lean, nervous, high strung, out of work and in the throes of a domestic chagrin, was operated upon without sufficient trial at medical treatment. He had a penetrating gastric ulcer in the middle of the lesser curvature. A saddle resection and gastro-enterostomy was done. He became delirious, vomited continually and died in seven days. This was a grave failure of surgical judgment.

I have refrained from mentioning the matter of surgical technic, for we know that surgeon's technic must be like Caesar's wife. Broadly speaking, we have three operations for benign stomach lesions.

(1) Pyloroplasty.

(2) Gastro-enterostomy.

(3) Partial resection.

There are many modifications of each. They all aim at two things: (1) draining the stomach, and (2) lowering the acidity. Often we cannot fit the operation to the lesion. First of all, we must save life. In several cases where resection should have been done we had to be content with pyloroplasty or gastro-enterostomy.

In the small series of cases presented, there have been 92 duodenal ulcers and 8 gastric ulcers. The gastric cases are too few to permit any deductions. In the gastric ulcers, 6 were resected boldly and an antecolic anastomosis done. These have all done well. In one case, with the ulcer very high on the lesser curvature, Balfour's operation was done. The ulcer was perforated with the cautery, sutured, and a gastro-enterostomy done. She has remained well after twelve years. The other case was the fatal one described above. In the duodenal ulcer cases, gastro-enterostomy was routinely done for many years. In recent years we have preferred pyloroplasty, taking care that the pyloric sphincter be ablated. Ten patients were subjected to pyloroplasty. These, too, are too few in number to permit any deductions. Eight have remained cured. One case in whom the ulcer was resected, continued to bleed. He went elsewhere and had a gastroenterostomy done. He continues to bleed at times.

Of the 82 duodenal ulcers treated by gastro-enterostomy, there has been only one mechanical failure; 86 per cent have been relieved of all symptoms and can eat anything; do not take soda or other medicine for indigestion. Of

these, 5 cases have occasional gastric distress after smoking or other indiscretions; 3 cases report themselves no better and no worse after the operation; 6 cases have developed jejunal ulcer. One of these perforated and died without operation. Autopsy showed the condition. This patient had a low acidity. The others have been relieved by taking down the anastomosis and resection.

While gastro-enterostomy gives satisfactory results in a large percentage of cases, it has one serious drawback, and that is the possibility of jejunal ulcer. This is a very real danger; one that causes most surgeons who are experienced in gastric surgery, absolutely to forbid a gastro-enterostomy on themselves should they suffer from duodenal ulcer. Any patient with a jejunal ulcer is in danger of his life. I now never do a gastro-enterostomy without the fear of this complication. From our limited experience we are now inclined to do partial resections.

In recent years more and more surgeons of experience are abandoning gastro-enterostomy. Partial gastrectomy is coming more into use for the cure of duodenal ulcer. It will be years before a true evaluation can be made of this procedure. The chances of anastomotic ulcer are greatly minimized, but they do occur, even after partial gastrectomy. Pyloroplasty leaves the digestive tract in a more anatomically normal condition than the other two operations. It is free from anastomotic ulcers and at worst, the patient will be in no worse condition than before the operation. It is said in the Bible that there is more rejoicing over the return to the fold of one sinner, than over the faithful ninety and nine.

Conversely, and particularly if you live in the same town, the grief over one anastomotic ulcer, outweighs the joy of ninety and nine successful cases.

How may we avoid failures in surgery? If someone could tell us beforehand which patients would do badly, we should gladly forego the operation.

There are certain signs and guide posts in selecting patients for gastric surgery that are most helpful. Family history of ulcer strongly suggests a constitutional tendency in that direction, and operations in these cases are apt to fail. The duration of the ulcer is an important point in deciding for or against surgery. All ulcer cases deserve long and competent medical treatment, and only when this has failed, should surgery be undertaken. The busy physician, the restless go-getter type of business man, and those addicted to alcohol and tobacco, all make poor subjects for gastric surgery. The best results are obtained by surgery, in cases having low acid, a slow emptying time, and a long history of gastric distress. Gastric surgery finds its best field in the middle-aged. The decision as to operation is so serious that it demands the cooperation of physician and surgeon.

As surgeons, we have found the gastro-enterologist most helpful. He works up the cases better than the busy surgeon, and discussion with him is worthwhile. As we have said before, the results of surgery may be brilliant, and occasionally they may be sad. It is in these sad cases that the association of the internist before, and particularly after the operation, is most comforting. If the internists are permitted to select the cases for operation, and to help in the necessary postoperative regime, we believe that gastric surgery will be the gainer.

OBSERVATIONS ON THE TREATMENT OF DIABETES WITH PROTAMINE INSULIN IN OFFICE AND HOSPITAL*

By HAROLD BOWCOCK, M.D.
Atlanta, Georgia

This preliminary report deals with the results obtained from the use of the slowly absorbed and consequently slow acting protamine insulinate, a very effective compound formed by the union of ordinary insulin hydrochloride with a protamine derived from the sperm of a trout. This compound was the most satisfactory of many which were made and tested by Hagedorn, Jensen, Krarup and Wodstup[1] at the Steno Memorial Hospital, Copenhagen. A report of the experiments of the Danish investigators and the results of their clinical observations during a period of two years was accompanied by a report of clinical experiences by Root, White, Marble and Stotz,[2] in Boston, and followed by reports from Hanssen of Copenhagen,[3] Lawrence and

*Received for publication June 10, 1936.

*A description of protamine insulinate, the method of mixing and administration, observations on dosage, occurrence and management of insulin reactions and remarks on diet will be published in the reprint of this abridged article.

*Protamine insulinate is not yet available commercially; I express my indebtedness to Eli Lilly & Company, my chief source of supply since February 1 of this year, and to E. R. Squibb & Sons for a smaller supply.

Archer of London,[4] Kerr, Best, Campbell and Fletcher in Toronto,[5] Wilder,[6] Sprague, Blum, Osterberg, Kepler and Wilder[7] of the Mayo Clinic, and Joslin, Root, Marble, White, Joslin and Lynch in Boston.[8] Other work has been reported.[9]

As Root and his associates have noted,

"Wide fluctuations in the level of blood sugar, with marked hyperglycemia on the one hand and hypoglycemia ("insulin reactions") on the other, represent one of the chief difficulties in the treatment of severe diabetes with insulin."

Protamine insulinate is an insulin compound with slow uniform action.

CLINICAL EXPERIENCE

The reports of Hagedorn and Root made it apparent that most of the studies of protamine insulinate would be conducted with hospital patients, and subsequent reports show the same trend. Consequently, it seemed advisable to discover whether it might be possible to adjust ambulant patients in school or business on the new insulin. Eleven patients, ranging in age from 5 to 45 years, were glad to try this experiment. In addition, seventeen hospital patients have been studied. The individual ambulant cases chosen showed difficult or poor control with regular insulin. Only patients who were intelligent, well trained and cooperative were entrusted with the problem. Ambulant patients kept their own daily charts, they mixed their insulin, tested and recorded their own urine tests at regular intervals at least four times each day and usually tested each individual voiding. Blood sugar determinations were made in the office laboratory; fasting, an hour or more after meals, four hours after meals and in the late afternoon. (Night blood sugar control was checked on hospital cases.) Hospital cases were chosen as controls to the method with ambulatory cases, or because of complications.

CHANGING FROM OLD INSULIN TO PROTAMINE INSULINATE

Ambulant cases were managed in two ways in changing to the use of protamine compound, depending upon the amount of time available for urine testing and blood sugar determinations. By the first method, which is probably safer for ambulant cases, the usual evening dose of regular insulin was changed to the same number of units of protamine insulinate. Since the new insulin is likely to produce a marked lowering in the blood sugar of the following morning the patient was advised that should the morning urine be sugar-free he should take about one-half of the usual morning dose of regular insulin; if the test should turn orange, take two-thirds of the usual morning dose; if red, take the usual morning dose of regular insulin. A noon dose of 10 units of regular insulin should be taken only in case the noon urine test is orange or red. If then, the first morning voiding shows sugar for three successive days, increase the evening dose of protamine insulinate by five unit stages and proceed as above. Blood sugar determinations are of no practical value during periods of the day when the urine contains sugar. In case it should become desirable later to attempt the change to a single morning dose of protamine insulinate, the usual evening dose of protamine insulin should be cut in half and the subsequent morning dose of protamine insulin should be a few units less than the total insulin units taken during 24 hours. This method will avoid serious acidosis and is not likely to occasion insulin reactions. The second method for ambulant cases is to change abruptly at morning to a single dose of protamine insulin equivalent to a few units less than the total insulin requirement for 24 hours. All urine specimens are to be tested and 10 units of regular insulin may be taken on the appearance of every red test. Subsequent days' test will show the advisability of increasing the size of the single protamine dose or of omitting the use of regular insulin. When all urine specimens are sugar-free during the 24 hours, interval blood sugar determinations should be made to discover the effectiveness of blood sugar control. It would seem that practically all diabetics can accomplish essentially normal blood sugar regulation by the use of protamine insulin alone or in conjunction with one simultaneous dose of regular insulin at a different injection site.

ILLUSTRATIVE CASES, AMBULATORY

It should be readily understood that the use of an unknown product must be approached with caution. The following cases have furnished data on the action of protamine insulin. Where results are not perfect, they are still so spectacular as to promise perfection. One should agree with Joslin[8] in his statement that this will be called the Hagedorn Era in the treatment of diabetes.

Case 1.—A 9½-year-old girl has had diabetes for almost four years. On a diet of 135 grams of carbohydrate daily, she required 2 or 3 doses of insulin daily for a total of 35 units or more. In recent months sugar-free specimens were rare unless accompanied by insulin reaction. Four areas of subcutaneous fatty atro-

phy have appeared on the thighs at the sites of insulin injections. The usual evening insulin dose of 13 units was changed to the same dose of protamine compound and the usual morning dose of 22 units of regular insulin was left unchanged. Almost immediately nearly all urine specimens became sugar-free. The most striking change was to morning sugar-free specimens. Later, the change was made to a single dose of 34 units of protamine insulin 60 minutes before breakfast each morning with the result that all voidings are sugar-free. There have been no reactions since the single dose has been adopted.

Case 2.—A woman, aged 21, has had diabetes since she was 6½ years of age; she has always been under excellent medical care. On a diet of 140 grams of carbohydrate and about 50 grams of fat, she was still obese. Her height was 58½ inches, weight 129 pounds. Her abdomen measured 36 inches and was so protuberant as to resemble a pregnancy. The edge of a soft smooth liver was palpable below the umbilicus, eight inches below the costal margin in the mid-clavicular line. Since the patient is a college student, it was inconvenient for her to take more than two doses of insulin daily; the dosage was 32 units of insulin in the morning and 36 units in the evening. Morning urine and many other specimens became orange or red on testing, and fasting blood sugars were always excessive. There was nausea every morning and frequent severe and prolonged headache. Mild acidosis was very frequent. She was changed to two doses of protamine insulinate of the same number of units. The morning urine specimens became sugar-free at once and the fasting blood sugar values became practically normal; on the other hand, the slow acting morning dose of protamine insulin showed very poor control during the day and on one occasion the blood sugar was 0.522 per cent two hours after breakfast. After repeated unfavorable tests, the usual morning dose of regular insulin was resumed and the evening dose of protamine insulin kept the same. On this routine, control was good: fasting blood sugar was 0.129 per cent; blood sugar two hours after breakfast, 0.146 per cent; 3 hours after lunch, 0.142 per cent. Six weeks after she started protamine insulin, nausea had ceased, headaches were rare, menstruation was more normal, weight was 126 pounds, the abdomen measured 31½ inches, a decrease of 4½ inches, and the liver was no longer palpable, although there was some dullness to percussion three finger breadths below the costal margin. Hanssen[8] has described such liver changes with protamine insulin.

Case 3.—A male physician, aged 33, has had diabetes for three years. During the past year control has been very difficult and there have been many reactions, with insulin dosage as high as 120 units daily. On a diet with 150 grams of carbohydrate he was given 30 units of protamine insulin in place of a like amount of regular insulin in the evening, and he received his usual dose of 40 units of regular insulin each morning. In several weeks it was possible to reduce the morning dose to 20 units of regular insulin. Later, the night dose of protamine insulin was reduced to 28 units and the morning dose was changed to 16 units of protamine compound. Fasting blood sugars of 0.059 per cent, 0.066 per cent and 0.078 per cent have been obtained without reaction. Other blood sugar values throughout the day were perfect or fair, rarely bad. The insulin dosage was then changed to a single dose of 44 units of protamine insulin each morning. On this routine he is usually sugar-free throughout each twenty-four hours, with normal blood sugar regulation. Occasionally, for a period of about four hours around midday, he shows hyperglycemia and a small amount of sugar in the urine. His blood sugar at 2:00 p. m. was 0.160 per cent; at 4:00 p. m. 0.1 per cent; at 10:00 p. m 0.065 per cent, fasting, 0.12 per cent.

PRIVATE HOSPITAL CASES

Case 4.—A man of 54 years has had very mild diabetes without any attempt at control for seventeen years or more. Following an injury he developed gangrene with infection of a great toe, accompanied by marked swelling of the toe, fever, hyperglycemia, and sugar in the urine. X-ray showed destruction of the distal joint with bone debris. With conservative treatment, a diet containing 140 grams of carbohydrate and a single dose of protamine insulin, 20 units, each morning, he has been constantly sugar-free for seven weeks. Blood sugars are: fasting, 0.101 per cent; four hours after breakfast, 0.112 per cent; one hour after lunch, 0.157 per cent; four hours after lunch, 0.131 per cent; midnight, 0.118 per cent. There have been no insulin reactions. The treatment of the toe has consisted of bland moist dressings, heat from an electric globe, and daily soaking for 45 minutes in a solution containing 5 grains of potassium permanganate to one quart of water. The improvement of the toe has been so remarkable that amputation has been deferred from day to day. A recent x-ray shows no bone debris; there is definite new bone formation, partial ankylosis of the joint and shortening of the toe. There is no drainage and tissue swelling has almost disappeared.

Case 5.—A man of 49 years has had diabetes for sixteen years. He has always received a liberal diet and 15 to 18 units of insulin daily. For sixteen years he has been an addict to a regular dosage of 15 grains of morphine by hypodermic daily and has been declared incurable in this habit. During the past few years he has taken for periods of several months large amounts of cocaine hypodermically. For the past month he has been under treatment for a rather extensive infection involving soft tissues, muscles and tendon sheaths of the palm of the hand, about thirty boils, and at the beginning, in addition to morphine, he was taking more than 40 grains of cocaine by hypodermic daily. His insulin dosage when he was first seen was 18 units of regular insulin in the morning and 10 units in the evening. He showed some sugar each day and rather marked fasting hyperglycemia. With 30 units of protamine insulin, one dose each morning, he remains constantly sugar-free with blood sugars of: fasting, 0.125 per cent; 30 minutes after breakfast, 0.154 per cent; at 4:00 p. m., 0.08 per cent; at 4:00 a. m., 0.158 per cent. His carbohydrate intake is slightly over 200 grams daily. Cocaine has been reduced to about 8 grains daily.

EXPERIENCE WITH WARD HOSPITAL PATIENTS

Dr. Albert Lewis, Resident in Medicine, Grady Hospital, Emory University, has given protamine insulinate to eleven hospital patients ranging in age from 14 to 57 years, for the most part uncomplicated but exhibiting difficult control with large doses of regular insulin. Several

have been satisfactorily controlled with one dose of protamine insulin daily. Three have required a simultaneous injection of 10 to 15 units of regular insulin at a different site once daily. A woman, 31 years of age, showed poorer control on protamine insulinate than on regular insulin in spite of the fact that she received ten units more of the protamine compound than the combined unit dosage of regular insulin. No case of coma has been treated with protamine insulin, but the Mayo group has described a method.

A number of patients are now being tested with calcium and zinc protamine insulin compounds with the hope of still greater success.

SUMMARY

Protamine insulinate exhibits distinct advantages over regular insulin. Most patients can accomplish perfect control with a single dose daily. Almost perfect blood sugar regulation throughout the twenty-four hours can be secured with a single dose or a single dose plus a small simultaneous dose of regular insulin. Insulin reactions are less likely to occur and are slower in onset, giving the patient more time to take the appropriate measures for counteracting the hypoglycemia. Complicated cases of diabetes may have the benefit of more normal control. The unpleasant symptoms of hyperglycemia with its accompanying tendency to acidosis occurring in some patients may be avoided. Hepatomegaly due to fatty infiltration of the liver may be corrected. Well trained cooperative office patients can secure the benefits of protamine insulin by observing caution and care during the period of adjustment, provided the required insulin dose is not too great. In other words, with practical control and adequate cooperation, a diabetic may look forward to the benefits of essentially normal carbohydrate metabolism.

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ARTIFICIAL FEVER THERAPY*

By Roy D. McClure, M.D.,
Detroit, Michigan

William H. Welch[39] wrote in 1888:

"There have been in all ages enlightened physicians who have held the opinion that fever is a process which aids in the elimination or destruction of injurious substances which gain access to the body. * * * The doctrine of evolution indicates that a process which characterizes the reaction of all warm blooded animals against the invasion of harmful substances has not been developed to so wide an extent and is not retained with such pertinacity without subserving some useful purpose."

Welch further says:

"We have found that animals may be kept at high febrile temperature for at least three weeks without manifesting any serious symptoms."

He advanced in 1888 the hypothesis that the increased oxidation which results from fever aids in the destruction of injurious substances and

"according to this view the fever producing agents *light the fire which consumes them.*"

Such a fire may prove injurious also to the patient and may require the controlling hand of the physician. He ends his lectures with:

"Unproven and untangible as the hypothesis may seem to some, no apology is needed for bringing to your attention a conception of fever, in favor of which much can be adduced and which, if true, is of fundamental importance, both theoretically and practically."

The time and means of testing this theory have now arrived. We now have this great opportunity because of the ability to create a high body temperature without the aid of disease.

With artificial fever therapy a patient's temperature may be held at 107 degrees for five hours for a series of treatments with no apparent ill effect, provided certain environmental factors

*Read in Section on Surgery, Southern Medical Association, Twenty-Ninth Annual Meeting, St. Louis, Missouri, November 19-22, 1935.

*From the Henry Ford Hospital.

are established and maintained. This has the advantage, of course, that there is no toxemia from bacterial or parasitic products.

To Dr. Julius Wagner-Jauregg,[38] of Vienna, belongs the credit for directing thought toward fever as a therapeutic agent. Some one has aptly termed this fever as "friendly fever." Wagner-Jauregg observed the improvement in cases of dementia paralytica who contracted malaria. Soon it was believed by many that it was the elevation of temperature and not the disease that caused this improvement. Safer standardized strains of malaria were developed and widely used for producing fever. Inoculations of rat bite fever[14 24] and relapsing fever were tried.[18 33] Typhoid vaccine and other foreign proteins were used. Prolonged hot water baths, hot air treatments, radiant heat in electric light cabinets and the infra red rays were tried and still the search proceeded further.

The problem became more clear-cut as time went on. It was to produce a fever of any desired degree up to say 107 degrees and hold it there as long as was desired, to remove the heat promptly if indicated and above all not to leave the patient with any harmful resulting disease or permanent tissue damage at the end of the treatment.

Diathermy machines and radiotherms proved of value. Willis R. Whitney, of the General Electric Company, noted that men working near the wireless short wave sending tubes developed fever. Whitney developed a special machine for sending these waves into animals and then into humans with marked fever production. Charles F. Kettering, of the General Motors Corporation, became interested, with Dr. Walter M. Simpson, of Dayton, in the possibilities of an air-conditioned cabinet for producing fever and they have done much toward its perfection.

The first important observation made after prolonged hot water or hot air baths, or the use of any other fever-producing mechanism, was the exhaustion suffered by the patient. The patient, of course, perspired profusely and unless given large quantities of water to drink would lose pounds of weight. Even if sufficient water was given to maintain his weight, the exhaustion lasted for several days. It was then realized that he lost not only water, but also salts in the perspiration, mainly sodium chloride, as shown by the drop in blood, and especially tissue, chlorides. Accordingly common salt was placed in the water he drank during the treatment, and miraculously after this addition the patient could go home in many cases immediately after his temperature had returned to normal without any signs of heat exhaustion.

At the Ford Motor Company plant in Detroit with 60,000 or 70,000 men working, on very hot days between three and four hundred men formerly reported to the first aid stations with all grades of heat exhaustion. Here now, as in many factories, it is the custom in the foundries, rolling mills, and wherever there is excessive heat to have salt tablet dispensing machines by each drinking fountain. When a man goes to the fountain for a drink of water he takes with it a five-grain salt tablet. One day, shortly after this system was in effect, there were only four heat prostrations in the entire plant with an official outside temperature of 104 degrees. At one time there was an increase in heat exhaustion cases and it was found to be due to the fact that one of the workmen had started the rumor that these tablets reduced sexual power. The absurdity of this rumor was reported to the men and use of the salt was resumed. During the construction of the Boulder Dam[8 36] the average daily maximum temperature in the summer of 1931 was 109 degrees, and the average mean temperature was 106 degrees. In that year there were 150 cases of heat exhaustion with 17 deaths. In the following years by the use of salt and proper sanitation there were no deaths from this cause, and the number of cases of heat cramps and exhaustion were reduced to a minimum.

The Kettering hypertherm, which we are using for fever induction and maintenance and to whose development we have referred above, has been described by Kendall, Webb and Simpson.[23]

During the course of the treatment, the patient usually drinks from four to six liters of 0.6 per cent sodium chloride solution. This abolishes the sense of fatigue and exhaustion and practically eliminates the nausea and vomiting, abdominal cramps and muscular twitchings, which are occasionally seen when this precaution is not taken. It usually takes from 30 to 90 minutes to raise the rectal temperature to 105 or 106 degrees, and it is particularly important, as Dr. Simpson emphasizes, that a trained technician be in constant attendance during the entire treatment. We also feel that this type of treatment is a hospital procedure, for one must be prepared to hospitalize the patient immediately should the indication arise.

The simplification of the apparatus, the removal of hazards inherent in certain other phys-

ical methods, and the supplying of large quantities (2 to 4 liters) of sodium chloride solution (0.6 per cent) by mouth during the treatment to replace chloride loss have converted this form of therapy from one requiring protracted hospitalization to one in which the patient is usually able to return to his work on the day following treatment, unless the extent of his disability makes hospitalization desirable.

The restlessness which appears during a treatment apparently as a result of these chemical changes may be quite satisfactorily controlled by the ingestion of sodium chloride and calcium gluconate and by the administration of properly selected sedatives. The leukocyte count[4] has been found to show an initial reduction of 15 to 30 per cent during the first and second hour of treatment. This is constantly followed by a leukocytosis which may reach a maximum of 80 per cent above the initial figure and occurs about the sixth to ninth hour following the beginning of the treatment.

The cases we have treated during the past two years are shown in the following table:

CASES TREATED BY HYPERTHERMS IN THE LAST TWO YEARS

Disease	Patients	Treatments
C.N.S. syphilis	72	583
Eye cases	48	131
Pelvic inflammatory disease	41	104
Rheumatoid arthritis	29	148
Gonorrheal arthritis	18	57
Gonorrheal urethritis	31	88
Multiple sclerosis	14	88
Chronic encephalitis	7	49
Chorea	4	19
Malignancy	8	38
Osteomyelitis	4	28
Miscellaneous	21	74
Total, 24 months	289	1405

GONORRHEA

In some of our early cases, failures resulted so far as the cure was concerned because of our lack of knowledge of the exact amount of treatment required. In our early cases of gonorrheal urethritis the peak temperature and the duration of the treatment were set rather arbitrarily with the result that there were many failures. Boak, Carpenter and Warren[7] have determined the thermal death point in over a hundred strains of gonococci. As a result of their work and that of others, it is very evident that if satisfactory results are to be obtained, that is, if the thermal death point were the only important factor (undoubtedly other powers of resistance are called out), the temperature must be maintained at high levels, 106 to 107 degrees for periods of six to eight hours, during each treatment. The number of treatments necessary will, of course, be variable, but it is the experience of many workers that with this particular type of infection a large percentage of those who complete the series of treatments will be made well. It is the observation of our group that the complications such as gonorrheal arthritis, epididymitis and ophthalmitis, yield promptly to the treatments.

As the result of the treatment of a series of twenty-one cases of gonorrheal urethritis in our clinic, Ormond[29] has reported the following conclusions:

(1) Treatment practically always has a favorable influence on the disease, and those who follow through to the completion of the course are in the majority of cases cured.

(2) The favorable effect of the treatment of complications is striking. Arthritis and epididymitis yielded promptly, and in one case of gonorrheal ophthalmitis which complicated, the cure was effected after one treatment.

(3) A temperature of 106 to 107 degrees in most instances has been well tolerated.

(4) An interval of three to four days between treatments is probably the optimum.

(5) The duration of treatment should probably not exceed six hours of sustained high fever.

GONORRHEAL ARTHRITIS

C. L. Mitchell, of the Henry Ford Hospital, has reported a series of sixteen patients with gonorrheal arthritis who were given fever therapy. Of these, nine were reported as well, four as improved, and three who refused to take a complete course of treatments were found to be untraceable. In some instances there was complete, or almost complete, relief from symptoms following the first treatment and from the experiences with these patients it is very definitely felt that fever therapy alone is often sufficient to effect a complete cure. The chronic cases are improved, but the treatments should be supplemented by bakes and massages, insufflation of air into the joint, with graduated exercises and support with appliances.

The consensus of opinion of a great many workers seems to be that a satisfactory result may be obtained in a very high percentage of the cases of gonorrheal arthritis. In some instances where joint changes have taken place previous to the treatment additional surgical measures may be necessary.

INFECTIOUS ARTHRITIS

In the case of acute infectious arthritis, the results are not so striking as in gonorrheal arthritis. In our series of thirteen patients with acute infectious arthritis, six received prompt and satisfactory relief in from one to four treatments. Four patients had relief from pain, but suffered residual joint disease, and three derived no benefit whatever. Most patients with acute arthritis tolerate fever therapy very well and are benefited by frequent and long treatment. In the case of chronic infectious or atrophic arthritis, Stecher[34] reports a group of 33 patients. Of these, eleven showed distinct and progressive improvement, but none was considered cured. The improvement consisted of decrease in pain and stiffness and an increase in the ability to be up and about. Nine other patients in this group showed moderate improvement, as judged by greater comfort and improved general health without any appreciable increase in activity. Thirteen patients received no apparent benefit and the treatments were discontinued. As contrasted to the other group, the patients with chronic infectious arthritis frequently tolerate fever treatments rather poorly and must be handled more carefully.

OSTEOMYELITIS

We have treated one case of extensive osteomyelitis of the bones of the face and skull which showed no improvement whatever from the treatment. Another patient who was treated because of osteomyelitis of the inferior margin of the left orbit which followed bilateral Caldwell-Luc operation, had the disease process arrested and made a satisfactory recovery. It is too early to evaluate the part played by fever therapy.

SARCOMA

H. P. Doub,[10] who has supervision of our fever therapy, has reported an interesting case of sarcoma of the clavicle which was treated by radiation and fever therapy. The fractured clavicle healed, the tumor mass has disappeared, the patient is back at work and the result has been beyond anything that we could have expected.

SYPHILIS

Dr. Frank Menagh, of our group, has reported very satisfactory results in the treatment of a selected group of patients with various types of luetic infection. I shall quote directly from his recent report:

"Anyone who follows the treatment of syphilis over a period of 15 years gradually accumulates a group of problem patients who do not respond to the usual treatment with arsenicals, bismuth, mercury and iodide. For the last ten years we used the malarial type of fever to good advantage with some of this group, but anyone who has used malarial therapy knows that it has certain grave disadvantages, one of which is that it necessitates the hospitalization of the patient for a considerable period of time. This not only entails great expense, but it takes the patient away from his job and places upon him a stigma that may make it exceedingly difficult for him to establish himself again in his social group. This, to my mind, is an extremely important consideration and every effort should be made to keep these patients normally active.

"A group of 25 such patients has been given the new artificial fever therapy. There were in this group 20 males and 5 females. They ranged in age from 17 to 63 years, with an average of 41 years. These patients had been under observation and treatment by us for an average period of 4 years and 4 months, the longest period being over 10 years. With many of them we had about reached the limit of our resources. These were given an average of 10.3 treatments each, a few receiving more than 50 hours of fever. Twenty-one were given additional anti-luetic therapy.

"As a result of treatment, this especially refractory group showed:

Improved	22
Unimproved	2
Dead	1

"The one that died, although he had had no demonstrable syphilis, was found to have had in addition a brain tumor. This was a very interesting case, but time does not permit of its discussion.

"The two unimproved patients were diabetics, with diabetic pain and ataxia. They were thin, emaciated individuals, and did not stand the fever well.

"In the improved group were 11 patients with central nervous system syphilis of the parenchymatous type, that is, positive spinal fluids with paretic gold curves, some of them with mild mental changes. This group did very well. Those with mental symptoms all improved, and at the present, one year after the end of treatment, none of them can be considered clinically active. This was the group that through the years had given us the greatest concern.

"There were six cases of tabes dorsalis, one of these with partial optic atrophy. The optic atrophy was arrested and apparently improved somewhat, due perhaps to the clearing of edema. I do not believe that any destroyed nerve fibers were ever regenerated.

"The remaining five cases who improved never had positive spinal fluid findings. This group consisted of two cases of interstitial keratitis that may well have cleared with the usual treatment, but who had no recurrences after fever, one case with a peristent strongly positive blood Wassermann reaction that promptly became negative and one of syphilis associated with epilepsy, with no attacks in the year since treatment, and one case of secondary syphilis that was treated both with fever and the usual chemotherapy."

GENERAL PARESIS

Under the direction of Dr. T. J. Heldt,[17] at the Henry Ford Hospital, this form of therapy

has been used in treating twenty-two cases of general paresis, and a group of seven miscellaneous cases, including chronic encephalitis, Parkinson's disease, and one case of encephalomyelo-radiculitis. Dr. Heldt reports that:

"In general paresis, this form of hyperpyrexia offers another effective means of arresting and sometimes staying the ravages of parenchymatous neurosyphilis. Improvement and 'social recovery' of the patient depend largely upon the degree of involvement at the time treatment is undertaken. In general, results fall roughly into three simple groups and percentages.

"Socially recovered—33 1/3 per cent
(meaning ability to continue at work or return to it).

"Improved—33 1/3 per cent
(meaning ability to be cared for extramurally, although unable to return to productive labor).

"Unimproved—33 1/3 per cent
(meaning failure to improve and requiring continuous hospitalization)."

Dr. R. J. Needles,[41] of our staff from the Ford Rubber Plantation in Brazil, reports that in four years only one case of neurosyphilis developed in spite of the fact that 31.8 per cent of 6,823 Kahn and Eagle tests were positive for syphilis. Since malaria is endemic in this region, 38 per cent of 38,786 smears were positive for malaria, the range being from 30 to 70 per cent in scattered villages.

"From these facts it is believed that endemic malaria influences favorably the incidence of neurosyphilis."

CORNEAL ULCERS AND IRITIS

In the field of ophthalmology, some very favorable results have been obtained. Dr. E. L. Whitney,[40] of our staff, has reported prompt healing of chronic corneal ulcers after fever therapy and in some instances the fever treatment has hastened healing where the local measures produced little progress. Eight cases of corneal ulcer were treated with most satisfactory results. In addition to this, six cases of acute iritis were treated with satisfactory results in the majority of cases. It was felt undoubtedly that recovery was hastened, but it was also felt that further observation would be necessary before the final opinion could be reached as to the probability of recurrences in the condition.

PELVIC INFLAMMATORY DISEASE

In our own clinic, Smeltzer[35] has reported the treatment of twenty-three cases with pelvic inflammation. Of this group, seventeen had what was considered an adequate amount of treatment, and of these, twelve were improved, three showed no improvement, one had an exacerbation of symptoms, and one died. There were seven patients with gonorrheal urethritis, cervicitis, and salpingitis, four of whom were improved by the treatment, one showed no improvement, one had an exacerbation of symptoms, and one died. Of those with non-specific pelvic inflammatory disease, four were treated, three showed improvement, and one no improvement. Four cases of post-abortal infection were treated and of these, three showed improvement and one was not improved.

In the experimental field, Major, Doub and Hartman[26] in our laboratory have reported the treatment of dogs inoculated with human tuberculosis with what were apparently fairly satisfactory results. Of the eight dogs treated, seven had a definite diagnosis of pulmonary tuberculosis as determined by x-rays and smears from the trachea. In the other one, the diagnosis was questionable. Of the eight treated, four died, probably as the result of vascular collapse. The dogs which recovered were well nourished, afebrile, and negative for acid fast bacilli in the trachea smears, and had negative x-rays of the lungs fifteen to twenty-two weeks after the inoculation.

COMPLICATIONS

Unless the patient is kept carefully covered with light cotton blankets, vesicles are rather prone to appear, which are undoubtedly the result of the excessive heating of droplets of perspiration. This complication may be avoided by ordinary precautions. Not infrequently when the body temperature is raised to 106-107 degrees and kept there for considerable time, herpes of the lip will develop, which are usually very transient and respond quickly to treatment. Nausea and vomiting were complicating factors in some of the earlier cases, but as stated previously, these symptoms may be avoided to a large extent by the administration of sodium chloride solution. Where this precaution is not taken, tetany will occasionally develop as a result of the production of alkalosis, and should this occur, it can be relieved by the administration of calcium gluconate solution, given intravenously, or by the inhalation of carbon dioxide and oxygen. It is our practice to keep an apparatus for the administration of carbon dioxide and oxygen available at all times for use of those patients who develop periods of

apnea and cyanosis with circulatory collapse. In a patient whose temperature went to 108.5 degrees F. typical shock symptoms appeared, but these cleared up rapidly with treatment and the patient left the following morning for football practice.

PATHOLOGICAL CHANGES

In our series of cases there have been two deaths, one occurring ten days after the last treatment.[22] This patient was being treated for pelvic inflammatory disease. She was two months pregnant. Autopsy revealed degeneration of the chorion with intra-uterine hemorrhage; hemorrhagic pneumonia; marked granular and hyaline degeneration of the zona fasciculata of the adrenals; hemorrhagic encephalitis; ring hemorrhage about the vessels in the base of the brain and acute parenchymatous degeneration of the liver and kidneys.

The other patient who died was one who was being treated for central nervous system syphilis. It had been felt, before treatment, that he possibly had a brain tumor which might be accounting for the Jacksonian type of epilepsy which he exhibited. He had eleven treatments and all were well tolerated. Following the last treatment, however, he lapsed into a coma and died about twenty hours later. Autopsy findings revealed syphilitic aortitis; partial occlusion of the orifice of the right coronary artery; a glioma of the cerebrum with cyst formation; hemorrhagic encephalitis at the base of the brain; a bronchopneumonia with edema of the lungs; vascular and granular degeneration of the zona fasciculata of the adrenals; acute parenchymatous degeneration of the liver and kidneys and chronic catarrhal cholecystitis.

As a result of these findings and of those present in experimental animals, the conclusion was reached that the changes which may occur are:

Engorgement of blood vessels, especially the capillaries; hemorrhage and degeneration. The most vital changes were those seen in brain, amounting in some instances to hemorrhagic encephalitis; those in the lung constituted hemorrhagic pneumonia and those in the adrenals were characterized by degeneration in the cortex with hemorrhage. In the experiments on animals, it was felt that death occurring during or immediately after treatment was due to vascular collapse.

CONCLUSIONS

(1) Artificial fever therapy is proving itself to be an important additional weapon against certain diseases.

(2) Adaquate fever therapy is not a simple therapy and to be safely given demands special training of nurse and doctor.

(3) It is natural that this promising field invites exploitation by unskilled and unscrupulous persons.

(4) We feel that in its present state of development it is decidedly not an office procedure, but that it should be attempted only in a hospital. As much care should be taken in the work-up of the patient and in the study of indications and contraindications as for a major surgical operation.

(5) A specially trained nurse must be with the patient every minute during the seven-hour treatment.

(6) While the usefulness of fever therapy in the treatment of gonococcal infections, syphilis, and certain forms of arthritis has been demonstrated, its application to many other diseases is still in an experimental phase. If the investigations in fever therapy can be kept on a high scientific plane, it seems probable that it will provide a valuable therapeutic adjunct.

(7) At the present time there are appearing in our medical journals advertisements of fever-producing machines for office use. Nothing is so apt to discredit fever therapy as this indiscriminate use under the belief that it is an innocuous thing. This tendency is very like that following the indiscriminate use of the roentgen ray on its introduction with its dire results, which slowed up for a time its rightful development.

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AN EVALUATION OF THE GONOCOCCUS BOUILLON FILTRATE (CORBUS-FERRY)*

A STATISTICAL REPORT OF 10,000 CASES

By BUDD C. CORBUS, M.D., F.A.C.S.
Chicago, Illinois

In the fall of 1934 the gonococcus bouillon filtrate (Corbus-Ferry) was placed on the market. Since that time considerable experience has been accumulated by others than those originally engaged as collaborators.

In order to evaluate this experience the following questionnaire was sent to all members of the American Urological Association and the American Neisserian Society:

(1) Have you had any experience with the Corbus-Ferry bouillon filtrate? Yes..... No.....

(2) Did you use it in combination with other forms of treatment? Yes.....No.....

(3) Were the results more favorable than with any other form of treatment in acute infections? Men..... Women..... In chronic infections in men?..... Women.....

(4) Have you followed the directions as to dosage as given by the manufacturers, or have you modified the dosage to suit your own experience? Yes..... No.....

(5) How many cases have you treated?.....

(6) Have you had any complications? Yes..... No.....

(7) If you had any complications, what were they?

It is obvious that an opinion based on the experience of this group would be of immense value in the future clinical application of the gonococcus bouillon filtrate.

Since September 3, 1935, the date on which the questionnaires were mailed, there have been 478 replies from both groups of physicians, comprising 9,662 cases treated.

In order to clarify the questionnaire, each answer has been studied carefully and tabulated in the following order:

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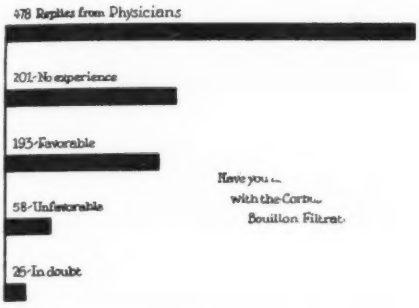
*Read in Section on Urology, Southern Medical Association, Twenty-Ninth Annual Meeting, St. Louis, Missouri, November 19-22, 1935.

QUESTION 1



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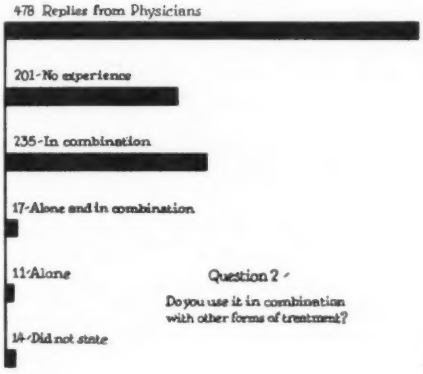

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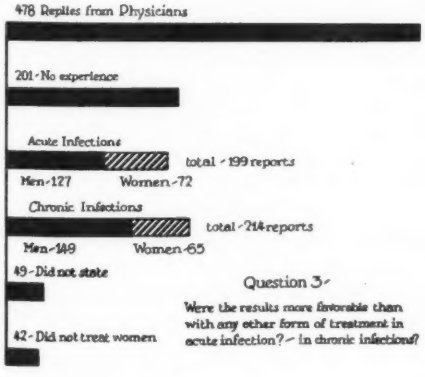

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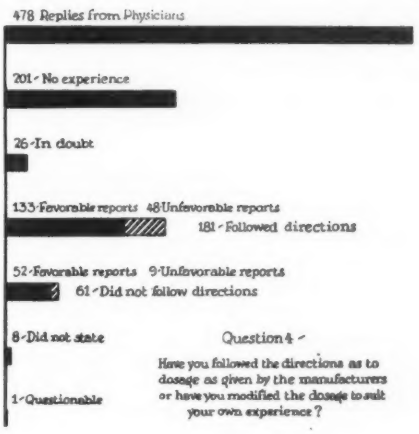
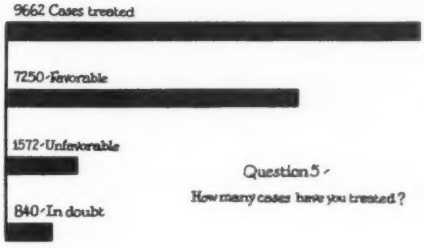
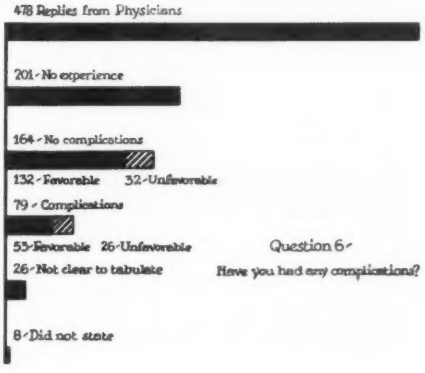

478 Replies from Physicians
201 - No experience
26 - In doubt
133 - Favorable reports 48 Unfavorable reports
181 - Followed directions
52 - Favorable reports 9 - Unfavorable reports
61 - Did not follow directions
8 - Did not state
1 - Questionable
Question 4 -
Have you followed the directions as to dosage as given by the manufacturers or have you modified the dosage to suit your own experience?

QUESTION 5



QUESTION 6


478 Replies from Physicians
201 - No experience
164 - No complications
132 - Favorable 32 - Unfavorable
79 - Complications
53 - Favorable 26 - Unfavorable
26 - Not clear to tabulate
8 - Did not state
Question 6 -
Have you had any complications?

QUESTION 7

Complications occuring in 193 favorable reports on Bouillon Filtrate, representing 5,141 cases.

Abscess, prostatic	2	
Abscess, urethral	2	(One observer states that Bouillon Filtrate seems to be of benifit in this)
Anaphylaxis	6	
Arthritis	2	
Epididymitis	22	(One observer states there is less epididymitis with than without Bouillon Filtrate)
Epistaxis	1	
Hematuria and dysuria	1	
Iritis	1	
Oedema, angio-neurotic	1	
Oedema, labia	1	
Prostatitis	9	
Reactions, severe local	2	(Patients sufferers from hay fever)
Salpingitis, acute	1	

Question 7 (a)
If you had any complications what were they?

57 Complications

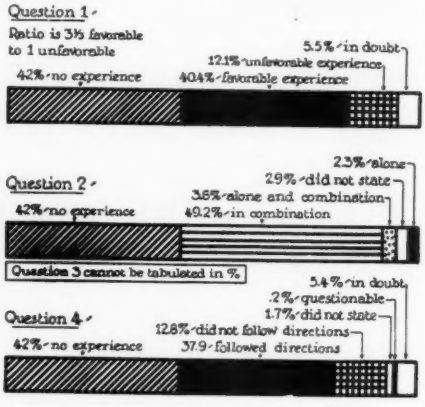
Complications occuring in 58 unfavorable reports on Bouillon Filtrate, representing 1,502 cases.

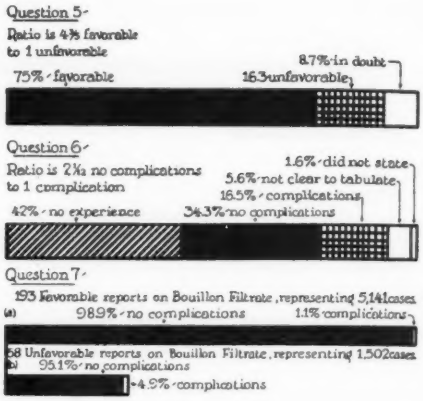
Abscess, paraurethral	2
Abscess, prostatic	11
All possible complications	1
Anaphylaxis	1
Arthritis	2
Bartholinitis	2
Epididymitis	26 (One observer reports four cases)
Hematuria	4
Prostatitis, acute	11
Pyosalpinx, acute	5
Rigors, fever, nausea, vomiting	1
Urethritis, posterior	4

Question 7 (b)
If you had any complications what were they?

74 Complications

TABULATED RESULTS OF SURVEY IN PERCENTAGES





Thirty-six physicians, reporting 1,611 cases, said their results were uniformly more favorable in acute and chronic gonococcal infections in men and women than with any other method.

Arthritis	1
Epididymitis	7
Inguinal adenitis	2
Prostatitis	2
Retention, acute	1
Urticaria	1
	14

Total number of cases treated.....1611
Total number of cases with complications..... 14

The complications herein reported are the same as those which occur in the general run of gonococcal infections with the exception of the anaphylactic reactions.

As there is no alien serum used in the manufacture of the toxin, we must presume that this reaction, when it occurs, is caused by a non-specific protein contained in the culture media, and in itself is not dangerous in the dosage given. However, an individual sensitive to the toxin should be treated by other methods.

In my early experience complications were frequent, but could always be attributed to overdosage.

During the last year over 175 cases of neisserian infections have been treated in our private practice. These include acute and chronic infections in men, women and children. The shortest time in which a cure was obtained in an acute infection was seven days in a male who noticed a discharge at 5:00 o'clock in the morning and received 0.1 c. c. bouillon filtrate at 2:00 o'clock in the afternoon of the same

day. The longest time that a patient was under observation was seven months.

In 50 per cent of these cases no other form of management was instituted except anterior instillations of a silver protein in 10 per cent solution administered once or twice a week in the office. Nothing was employed in the female except hot sitz baths and vaginal douches.

Complications, such as epididymitis, posterior urethritis, prostatitis and prostatic abscess, occurred in less than 3 per cent of all cases. In fact, the one case of prostatic abscess could easily be attributed to other causes. We have never seen an arthritis develop as a complication of the bouillon filtrate. On the other hand, we have seen many cases clear up completely in an exceedingly short time with the bouillon filtrate supplemented by prostatic massage.

The gonococcal bouillon filtrate is very toxic. Overdosage often results in edema with engorgement of the entire urethra, with attending complications such as posterior urethritis, epididymitis, prostatitis, vesiculitis and prostatic abscess.

During the last year the following directions in regard to dosage have been followed carefully in the management of acute and chronic neisserian infections in men and women. The results were very encouraging. However, the time of the cure has not figured in the end results.

The size of the first dose is in direct proportion to the duration of the infection, that is: the first week, 0.1 c. c.; second week, 0.15 c. c.; third week, 0.2 c. c., and so on. However, never commence treatment with an initial dose larger than 0.2 c. c. in a chronic case. Following the first dose, the size of the local cutaneous reaction should be used as a guide to future doses.

If the local tissue reaction after twenty-four hours is only two inches in diameter, increase the dose after seven days by 0.1 c. c. If the local tissue reaction is from two to three inches in diameter, do not increase the dose until the local tissue reaction after twenty-four hours is two inches in diameter or less. If the local tissue reaction is over three inches in diameter after twenty-four hours, decrease the dose by 0.1 c. c.

In order accurately to determine the size of the local tissue reaction after twenty-four hours it is suggested that the patient trace the size of the inflammatory area with tissue or toilet paper, bringing the tracing to the doctor at his or her next visit.

Reactions are less severe following the cutaneous injections of bouillon filtrate if the injections are placed on the posterior surface of the arms or anterior surface of the torso.

Using the size of the cutaneous reaction as a guide to future doses, it is advantageous to step up the dose often as high as 0.4 to 0.5 c. c., repeating the last dose at least twice after the patient is free from gonococci.

SUMMARY

Herewith is presented an analysis of the questionnaire which was sent to 850 physicians. There were replies from 478 physicians, 42 per cent of whom had no experience, 40.4 per cent had favorable results, 12.1 per cent claimed unfavorable experiences, while 5.5 per cent were in doubt.

The use of gonococcal bouillon filtrate in combination with local treatment seemed to be productive of the best results.

Chronic infections in men and acute infections in women responded best to the intradermal medication.

The directions in regard to dosage were followed in a large majority of reports.

In all there were 9,662 cases treated. The ratio of favorably treated cases to unfavorably treated cases was 4.75:1.

Thirty-six physicians, reporting 1,611 cases, stated that their results were uniformly more favorable in acute and chronic infections in men and women than with any other method.

As one would expect, the number of complications occurring in the unfavorably treated cases is higher than the number occurring in the favorably treated cases.*

55 East Washington Street

DISCUSSION (*Abstract*)

Dr. Rogers Deakin, St. Louis, Mo.—Dr. Corbus' stimulating presentation at the Memphis meeting of the American Urological Association several years ago of the early work with this filtrate, together with the somewhat contrary views as to the serological and immunological aspects of gonorrhea which Dr. Pelouze presented during the same program, led me to follow a series of cases in the Genito-Urinary Clinic of the Washington University Out-Patient Department during the following year.

Our experiences were never reported, and I must say an adverse report was given the manufacturer of the filtrate, even though there were instances where my clinical impression was favorable. When the oppor-

*In every instance where two approximate figures were given in the statistics, the smaller one was tabulated.

tunity was again offered last fall to repeat the work using the new product, I was quite agreeable. I determined this time to attempt a much more critical analysis of our results, with the feeling that clinical impressions are oftentimes not borne out by cold-blooded figures. During the past eleven months we have started 112 men on the filtrate. The mortality has been high, but remember that we are dealing with illiterate whites and Negroes in the main, most of whom have no interest in their troubles past the stage when it is no longer painful to urinate. Consequently, it has been difficult to accumulate a sizable group of filtrate and non-filtrate control cases in which the period of observation was entirely satisfactory. It is felt, however, that this occasion offers an opportunity to present our findings up to the present time.

We also initiated the routine use of complement-fixation blood tests at this time for two reasons: one, to clarify in our own minds its usability, and two, as a possible check on the clinical results obtained in this problem. During the year Mrs. Ebel, in Dr. Bronfenbrenner's department, has run 848 tests for us.

Even though I did not give each treatment personally, I assumed complete responsibility for the therapy instituted, so that the two seniors who were doing most of the actual work were carrying out in the main a routine type of local treatment in both the filtrate and control groups. The personal equation would, therefore, be that much more limited, and certainly subject to the same errors and limitations in each group.

We have prepared curves to show the behavior of acute cases in both groups, based on the disappearance of the gonococci, and have charted the percentage of positive smears obtained on successive weeks and months from each group. The non-filtrate groups showed a better curve than the filtrate groups. I fully appreciate that this represents but one phase of the case progress, but it is adaptable to representation in chart form and indicative of the course of the disease.

We have also contrast slides which show the behavior of the chronic gonorrheas with and without the filtrate in the same manner.

We have charts which show the clinical progress, complications and so on of the filtrate and non-filtrate groups. Here again, the filtrate groups as a whole suffered by comparison with the non-filtrate groups. The late rise in two of the curves may be explained by an occasional positive smear from recurrence, or possibly re-infection, at a time when most of the cases had been dismissed or had stopped of their own accord. One or two such positives in a relatively small group of smears creates a relative disproportion in the curve.

The clinical results obtained in the acute and chronic groups with and without the filtrate have been further subdivided according to the behavior of the complement-fixation test. An uneventful course from onset to cure is considered "O. K." A complication of any sort made the case "unsatisfactory," even though the clinical course, so far as time element or end result was concerned, proved satisfactory eventually. The percentage figures shown in the various groups need not, and should not, be given any consideration at this time.

The analysis of the cases proved most interesting. If the cases (72 in all) were divided simply into two groups, filtrate or no filtrate, there is no demonstrable difference in their clinical performance. Continue this analysis, but separate acute from chronic cases, and there is still no particular advantage to be gained so far as our results are concerned.

However, if the group is still further subdivided, so that the acute and chronic groups are considered according to whether their bloods were positive or remained consistently negative, again with or without the filtrate, it will be noted that in the acute group there is little if any difference in the clinical results. There is some slight indication that the acute cases with positive bloods do not do so well with the filtrate.

The most startling discrepancies appear in the chronic group, where a combination of positive blood and the filtrate therapy gave us a very low percentage of good results (11 per cent) and on the other hand the group with consistently negative bloods plus the filtrate gave a very high percentage (90 per cent) of clinically satisfactory results.

To see if this interesting fact were substantiated in any other way, I again resorted to a plotted curve of these two groups in question by their smears and obtained what I consider irrefutable evidence of the accuracy of our observations.

It would seem to me, therefore, that even though our series to date is small, the critical analysis to which these cases have been subjected warrants the conclusion that an individual with a chronic gonorrhea who has a positive complement-fixation had best not receive the filtrate; that a similar individual but with a negative blood should be benefited by its administration; and that what is most important of all, the acute case, in which we are all vitally interested, is perhaps better off without the filtrate.

Dr. Otto J. Wilhelmi, St. Louis, Mo.—My results are very much in accord with those found by Dr. Deakin. We ran a small series in several of my clinics here, and I was quite surprised to note that any foreign protein given intradermally gave us practically the same end result as was obtained with the Corbus-Ferry filtrate.

My results in private cases in the office were identical with those found in the clinics. We did notice, also, that, in acute cases, no matter whether the filtrate or a foreign protein was used, there was always an aggravation of symptoms which frequently resulted in posterior involvements such as epididymitis and prostatic abscess. Our work was done mostly with such proteins as "proteolac" and "lactigen," which were administered intradermally in the same amounts as the filtrate.

Treatment curves on (1) routine treatment, (2) treatment with Corbus-Ferry filtrate, and (3) treatment with foreign protein, showed little if any variation.

Dr. Corbus (closing).—I do not feel discouraged as to the ultimate success of the bouillon filtrate in the cure of gonococcal infections, as the failures were probably due in the main to misinterpretation of the directions. Each case should be highly individualized, as all subsequent treatments depend entirely upon the patient's reaction to the initial injection. The ultimate success in every case depends upon meticulous management, as no two cases are alike, nor do they make similar responses to the toxin.

I do not agree with Dr. Deakin concerning his use of the complement-fixation test as a control in the management of gonococcal infections treated with the bouillon filtrate. I cannot believe his work to be of

much value, as years ago we found, with many others, that the complement-fixation test was never positive in acute Neisserian infections unless complications were present. It has been our custom to use the test only as a diagnostic aid.

Dr. Wilhelmi states that his conclusions are similar to Dr. Deakin's. Failure to secure improvement in both acute and chronic infections were due, I think to a faulty method of administering the filtrate or to improper dosage. It should be given from at least four to six inches away from any previous site of injection. The reaction is best interpreted when the inoculations are given on the posterior surface of the arms or forearms and the anterior surface of the torso.

GRANULOMA ANNULARE*

REPORT OF UNUSUAL CASE

By W. F. SPILLER, M.D.
and
EMIL H. KLATT, M.D.
Galveston, Texas

The case to be reported presents typical lesions in many different parts of the body. They are found on the backs of both hands, the wrists, along the margins and dorsum of the fingers, over the extensor and flexor surface of forearms, around both ankles and the dorsum of both feet as well as around both knees, on the back of the neck and under the chin. In reviewing the literature, we are unable to find a report of another case with such an extensive involvement.

From an etiological standpoint we feel that it is of great interest, since the patient gives a history of association with a child, his cousin, who had similar lesions before the appearance of his first nodules. This child has since died, so there is no chance for a check on the lesions, although they are described as identical by the mother of this boy, who is a very intelligent woman.

A survey of the literature on this skin disease shows that the etiology is unknown. The earliest reports on granuloma annulare showed a strong belief that tuberculosis was the etiological factor, and a careful search was made to find this in the patient or in the family history.

There was no history of tuberculosis on either side of this boy's family, though he gave a history of having played with a friend who had pulmonary tuberculosis three or four years before. This association was over a period of one and a half years.

From studying our case and from reviewing the literature of this comparatively rare disorder, we are inclined to believe this to be a definite clinical entity that may be due to a specific micro-organism or possibly to the absorption of certain toxins emanating from any one of several sources, for example, infected tonsils. The writers believe that it would be less rare if it were tuberculous in origin, and that tuberculosis and granuloma annulare in the same patient are a coincidence. The question is certainly still a wide open one.

A boy, aged 7, was first seen in the dermatological department of John Sealy Hospital in July, 1935, being referred from the surgical department for a skin rash over the body. Examination of this rash, which was situated in the aforementioned sites, disclosed soft whitish well raised nodules and many circular, crescentic and linear forms. Many of the nodules were grouped in various shaped plaques, while others were fused, giving a beaded effect. The nodules which had enlarged peripherally with apparent depressed centers showed a brownish color in the central portion. This same pigmentation was seen in many of the plaques. The annular forms varied in size from 1 to 3 cm. in diameter. Lantern slides of this case demonstrate the multiple forms assumed by the lesions and its extensive distribution.

The patient's mother stated that this first appeared three years previously during the summer months as small nodules on the dorsum of the right hand and soon after on the left hand. These enlarged and formed rings, while new lesions continued slowly to appear. There was no itching or scaling of the lesions. During the last year they have increased very rapidly, involving the fingers, the dorsum of the hand, the forearm, elbows, and also appearing on the legs, especially around the ankles, the dorsum of the foot and around the knees. Then they appeared in large numbers on the back of the neck and in smaller number under the chin. The mother states that some of these lesions disappeared without treatment, leaving no scars, while new ones developed to replace the old ones. The child was apparently not suffering from the lesions, and since it was believed that they were a form of wart, a physician was not called.

The boy's family history was negative, though he gave a history of several attacks of influenza, quite a few attacks of tonsillitis, and an occasional attack of bronchitis. He had varicella only a short time previously and was operated upon for a right inguinal hernia about six months before.

He was normal in height for his age, though slightly underweight. There was no lymphadenopathy, tonsils were hypertrophic, the heart and lungs were normal, the abdomen was negative except for scars where hernia was repaired in the right inguinal region. The blood count, urinalysis, Wassermann and tuberculin (1-1000) tests were all negative. An x-ray of the chest was not made because of the negative tuberculin test.

The lesions presented by this boy were so typical of

*Read in Section on Dermatology and Syphilology, Southern Medical Association, Twenty-Ninth Annual Meeting, St. Louis, Missouri, November 19-22, 1935.

those of granuloma annulare that no other diagnosis was considered. A section of tissue which was taken for microscopic study showed that there is a slight hypertrophy of the epidermis, without other signs of abnormal changes in this layer. The marked tissue changes were found in the cutis, where there was a marked increase in the thickness of this layer, due mainly to the increase in collagen fibers. Found scattered throughout this material were abundant epithelioid and lymphocytic cells. The cells took on an arrangement which was suggestive of the so-called "Russell bodies" in several areas in the section; however, the feature of the central necrosis was either very early or absent. No giant cells were found; no perivascular infiltration was noted; the epidermis showed no marked changes. The clinical diagnosis of granuloma annulare was apparently substantiated by the microscopic findings.

Several sections of tissue were stained with acid fast stains and a thorough search of each was made for organisms, but none was found.

In treating this case we have used x-ray alone and no other therapy. On August 6, 1935, he received 100 kilovolts, 3 ma. at 10 inches distance for two minutes, 160 r unfiltered.

On August 23, he received 120 r; on August 27, 120 r; and on October 12, he received 160 r.

With this treatment many of the lesions have disappeared without scar formation, while many others have been greatly reduced in size and we are watching and expecting these to follow the course of those that have disappeared. If it is necessary, we shall supplement this therapy with some form of arsenic.

In summary, we have presented a case of unusual distribution which has all of the known etiological possibilities. We can only say that the etiology is unknown.

We are indebted to Dr. Harris Williams for the pathological work done in this case.

DISCUSSION (*Abstract*)

Dr. Clinton W. Lane, St. Louis, Mo.—The lesions of granuloma annulare in this patient were far more widespread than any I have been privileged to see or to find in the literature. According to the records at the Barnard Free Skin and Cancer Hospital, there have been nine proven cases of granuloma annulare admitted to the clinic. Three additional patients have been observed by me in private practice and a few others elsewhere. None of these approached in any way the wide distribution seen in this patient. One case, however, did present lesions on the arms and the back. In the others there were two or three areas usually limited to the distal portions of the extremities.

The clinical diagnosis of granuloma annulare is not particularly difficult. When present on the hands it does bear a close resemblance to the disease known as erythema elevatum diutinum. Many observers consider them to be the same affection. Darier believes the erythema elevatum diutinum of Crocker is merely a disseminated or grouped variety of granuloma annulare. The annular lesion of syphilis will at times cause some immediate confusion, but can be readily differentiated. The ringed form of erythema multiforme might occasion some delay in making a definite diagnosis, but the distribution, course, and histology differ from granuloma annulare.

A recent case at the Barnard Clinic was quite interesting. An irregularly oval nodular lesion on the forehead was diagnosed granuloma annulare by some and sarcoid by others. The color was yellowish brown rather than a bright red, much more like the sarcoid of Boeck. An histological section was desired, but the patient refused, and disappeared from the clinic after the request for a section.

The determination of the etiology is the most important point in a consideration of this disease. The battle is still raging as to whether it is a tuberculous skin lesion or not.

In 1933, Dr. Jeffry Michael read before the American Dermatological Association a most interesting paper on this subject. It contained a report of eight cases and gave a very extensive review of the literature. Much of the following material has been gleaned from this paper.

Dittrich was the only observer who has ever found acid-fast organisms resembling tuberculosis in sections. This was not confirmed by guinea-pig inoculation. In granuloma annulare, guinea-pig inoculation has been uniformly negative.

The relationship to generalized tuberculosis means very little. Michael reviewed 53 cases. In thirty-five there was no tuberculosis, eight had active tuberculosis, five were questionable, two had healed tuberculosis of the lungs, one tuberculosis of the bone, one questionable bone tuberculosis and one tuberculosis adenitis. Michael believes that the concomitant appearance of granuloma annulare with tuberculous skin disease elsewhere on the body is more important than with general tuberculosis. There are many more cases that occur in the non-tuberculous than in the tuberculous individual. It must be remembered, however, that tuberculosis may be present and not so pronounced as to be recognized clinically.

The tuberculin reaction varies, and in the majority of cases is negative. A negative tuberculin test is, of course, much more important in children in ruling out tuberculosis than in an adult. Tuberculin injections will occasionally cause the disease to disappear. This is not always evidence of a true tuberculous response, as it may be a non-specific effect.

Michelson gave these criteria on which a diagnosis of tuberculosis of the skin may be made. They are a definite history, the morphology of the lesion, the biopsy picture, the tuberculin reaction, blood culture study and guinea-pig inoculation. The two positive signs are, of course, the finding of tubercle bacilli *in situ* and recovering the organism after an injection into a guinea-pig. Up to the present time, we have very little evidence upon which to class granuloma annulare with the tuberculous diseases of the skin.

Dr. Lloyd W. Ketron, Baltimore, Md.—At the last meeting of the American Medical Association at Atlantic City, Dr. Goodman and I presented a paper on a histological study of granuloma annulare. In two unusual cases we were able to secure very early lesions in which, with the material from several other cases in our laboratory, we felt that we could trace the pathology of this disease from its earliest manifestation to its full development. Our conclusions were that the primary manifestation is degeneration of the connective tissue resulting in necrosis. This is followed by an infiltration of macrophage cells and later repair.

ACUTE ASEPTIC MENINGITIS*

By SAMUEL S. RIVEN, M.D.
and
WILLIAM L. FLEMING, M.D.
Nashville, Tennessee

In 1925 Wallgren[1] [2] called attention to a syndrome which he designated acute aseptic meningitis. As described by him the condition is characterized by the abrupt development of symptoms and signs of mild meningitis associated with a lymphocytic pleocytosis in the spinal fluid. The latter is sterile and otherwise essentially normal. The disease runs a short, benign course and occurs without relation to local suppuration (as brain abscess or mastoiditis, etc.) or systemic disease. Recovery is usually prompt, complete and without sequelae. Wallgren's observations have been abundantly confirmed by European observers,[3] [4] [5] [6] and a few reports have occurred in the American literature.[7] [8] [9] [10] [11] [12] The recent work of Armstrong and Lillie,[13] Rivers and Scott,[14] and Armstrong and Dickens[12] suggests the possibility that the disease may be due to infection with a filterable virus. The matter is of such interest as to warrant the report of three cases which were observed in the Vanderbilt University Hospital in the summer of 1935.

REPORT OF CASES

Case 1.—S. L., an unmarried Jewish saleslady, aged 23, was admitted to the Medical Service of the Vanderbilt University Hospital on July 6, 1935, complaining of a severe headache. Her illness began July 2, 1935, when she noticed slight drowsiness, generalized aching, and malaise. The following day she felt better except for a persistent, annoying headache, which by evening became so severe that she was unable to sleep. Nausea, vomiting and elevation of temperature (101°) were present on the third day of her illness and persisted to the time of admission to the hospital. The sensorium remained clear and her chief complaints on arrival in the ward were headache and slight stiffness of the neck.

The past history was irrelevant. The family history was of interest. A brother-in-law who lived in the same house with the patient had just been discharged from a tuberculosis sanatorium and his wife had been under observation for a period of eight months because of a minimal, active apical tuberculosis.

Upon physical examination the patient's temperature was 101° F., pulse 110, and respirations were 22. The patient was restless though drowsy. She lay in bed with her eyes closed and her hand pressed over the temporal regions. When aroused she complained of a violent headache and of pain in the cervical region. The general physical examination revealed no additional significant abnormalities. The blood pressure was 110/70. On neurological examination the following positive findings were noted: slight fullness of the retinal veins, moderate cervical rigidity, the presence of Kernig's sign on the right, and hyperactive deep reflexes.

A spinal puncture was performed on July 6, 1935. The cerebrospinal fluid pressure was found to be 40 mm. of water. Fifteen c. c. of fluid were withdrawn and examined. Globulin was found to be increased (Pandy 2 plus). There were 180 cells per cu. mm., 90 per cent of which were lymphocytes. No organisms were found either by examination of the stained centrifugalized sediment or by culture. There was no pellicle formation. The total chloride content of the spinal fluid was 554 mg. per 100 c. c.; the sugar was 40.2 mg. per 100 c. c. The Wassermann and Kahn tests were negative, as was the colloidal mastic test.

The red blood cell count was 4,500,000, the hemoglobin determination 14 grams, and the white blood cell count 11,300. The Wassermann and Kahn tests with blood serum were negative. A roentgenogram of the chest was normal. The temperature never exceeded 101° and became normal after two days in the hospital. This coincided with complete disappearance of symptoms. On July 8, 1935, a second lumbar puncture was done. The cerebrospinal fluid pressure was 50 mm. of water. There were 225 cells per cu. mm., 98 per cent of which were lymphocytes. The globulin test was positive (Pandy 2 plus), the sugar was 39 mg. per 100 c. c. and the total chlorides were 536 mg. per 100 c. c.. Cultures and smears again were negative.

Spinal fluid obtained on July 8, 1935, was injected intracerebrally into two monkeys and eight mice. A few of the mice developed cerebral abscesses and meningitis due to infection with a gram positive diphtheroid and were discarded. The remainder of the animals did not develop meningitis or other evidence of virus disease.

On July 15, 1935, a third lumbar puncture was done. The cerebrospinal fluid pressure was 60 mm. of water. The Pandy test for globulin was negative and the cell count was 25 per cu. mm.; all of the cells were lymphocytes. The chlorides were 704 mg. and the sugar was 50 mg. per 100 c. c. A fourth puncture on July 19, 1935, revealed a cerebrospinal fluid pressure of 50 mm. of water. The cell count was 8 per cu. mm. and a negative globulin reaction was obtained.

On July 22, 1935, sixteen days after admission to the hospital, the patient was discharged. The patient returned on October 1, 1935, and was still entirely well.

Case 2.—E. L., a Jewish school girl, aged 16, was admitted to the Medical Service of Vanderbilt University Hospital on July 8, 1935, complaining of a severe frontal headache. On the morning preceding admission to the hospital the patient developed a frontal headache, associated with aching of the eyeballs and photophobia. During the day the headache became quite severe and was associated with stiffness of the neck. She felt chilly and feverish and vomiting occurred. Of interest was the fact that her sister (S. L., Case 1), with whom she slept, had been admitted to the hospital two days previously with a similar com-

*Read in Section on Medicine, Southern Medical Association, Twenty-Ninth Annual Meeting, St. Louis, Missouri, November 19-22, 1935.

*From the Department of Medicine, Vanderbilt University Hospital, Nashville, Tennessee.

plaint. As in the case of the sister, exposure to tuberculosis had occurred.

Upon physical examination her temperature was 101° F., pulse 118, and respirations were 20. The patient was a well developed, well nourished young girl who complained of severe headache and stiffness of the neck. The general physical examination was entirely normal except for the presence of palpable epitrochlear and axillary lymph nodes. The blood pressure was 110/70. The neurological examination revealed slight cervical and lumbar rigidity and slightly hypoactive deep reflexes; Kernig's sign was present on the right and Babinski's sign was elicited on the left side.

A spinal puncture was performed July 8, 1935. The cerebrospinal fluid pressure was 60 mm. of water. Fifteen c. c. of clear fluid were withdrawn and examined. Excessive globulin was present (Pandy 2 plus). There were 56 cells per cu. mm., 88 per cent of which were lymphocytes; the sugar content was 39 mg. per 100 c. c. and the chloride content was 560 mg. per 100 c. c. The Wassermann and Kahn tests were negative. No organisms were found either on examination of the centrifugalized sediment or by culture. There was no pellicle formation.

Cerebrospinal fluid and filtered (Berkfeldt) nasal washings obtained July 8, 1935, were each injected intracerebrally into two monkeys and eight mice. A few of the mice, as in the experiment with material from Case 1, developed pyogenic cerebral abscesses and meningitis (diphtheroid contaminant). The remainder of the animals did not develop meningitis or other evidence of virus disease.

A blood culture remained sterile. The red blood cell count was 4,640,000 and the white blood cell count was 7,000 per cu. mm.; the hemoglobin determination was 14 grams per 100 c. c. A roentgenogram was made of the chest and was normal.

On the second day after admission to the hospital the temperature rose to 102° and remained elevated until the fourth day. With the disappearance of fever on the fourth day the patient became free of symptoms and signs of meningitis. On July 9, a second lumbar puncture was performed. The cerebrospinal fluid pressure was 155 mm.; globulin was present (Pandy 2 plus); the cell count was 303 per cu. mm., predominantly lymphocytes; the sugar was 57 mg. and the chlorides 668 mg. per 100 c. c. Cultures of the fluid remained sterile. On July 15 a third cerebrospinal fluid examination revealed that the cell count had fallen to 125 per cu. mm.; 91 per cent of the cells were lymphocytes. On July 19 a fourth lumbar puncture was performed. The cerebrospinal fluid pressure was 60 mm. of water, the cell count was 12 per cu. mm. and all of the cells were lymphocytes. On July 23, 1935, the patient was discharged from the hospital well.

*Case 3.**—R. S., a white man, married, an auditor, aged 28, was admitted to the Medical Service of Vanderbilt University Hospital on the evening of July 22, 1935, complaining of headache, nervousness and vomiting. His illness began the same morning, when he awoke with a frontal headache which gradually increased in severity until 2:00 p. m. of the same day, when he was forced to go to bed. He slept for about two hours, but on awakening the headache persisted and he began to vomit. He experienced chilly sensations and fever. The sensorium remained clear. The past history was irrelevant except for the fact that he had just returned from the eastern part of the State, where there had occurred several cases of poliomyelitis.

Upon physical examination, his temperature was 100.8° F., pulse 90, and respirations were 22. The patient was a slender young man who appeared acutely ill. When disturbed he was very restless and irritable. The general physical examination was otherwise entirely normal. The blood pressure was 135/70. The neurologic examination revealed slight but definite rigidity of the neck, slight edema of the optic discs and fullness of the retinal veins and hyperactive deep reflexes. Kernig's sign was present.

Shortly after admission to the hospital a lumbar puncture was performed. The initial cerebrospinal fluid was 95 mm. of water. Fifteen c. c. of fluid were withdrawn, which turned somewhat turbid on standing, but there was no pellicle formation. The cell count was 47 per cu. mm., polymorphonuclear leukocytes predominating; the Pandy test for globulin was positive (2 plus). The Wassermann and Kahn tests were negative. The colloidal mastic test was negative. No organisms were found either by examination of the centrifugalized sediment or by culture. Blood cultures remained sterile. The hemoglobin determination was 15 grams per 100 c. c., the red blood cell count 4,300,000, and the white blood cell count 4,000 per cu. mm.

A few hours later a second lumbar puncture was performed. The cerebrospinal fluid pressure was found to be 175 mm. of water. There were 49 cells per cu. mm. and all were lymphocytes. The test for globulin was positive (Pandy 2 plus). The sugar was 68 mg. per 100 c. c. and the chlorides were 640. A second culture of the spinal fluid remained sterile. The second lumbar puncture relieved the headache and vomiting. Intermittent fever continued for the next two days, the temperature never exceeding 101° F. However, he rapidly became free of symptoms and the abnormal neurological signs disappeared. On July 24, 1935, a third lumbar puncture revealed the cerebrospinal pressure to be 65 mm. of water. There were 119 cells per cu. mm. They were predominantly lymphocytes.

On July 24, a small amount of cerebrospinal fluid was injected intracerebrally into six white ("Swiss") mice with negative results.

On July 31, 1935, the patient was discharged from the hospital as cured.

COMMENT

In view of an increase in the number of reported cases of acute aseptic meningitis in recent years, a summary of the important clinical features of the disease as described in the literature and observed in our cases will be given. The average duration of illness is one week, with extremes of 3 days to 3 months. The disease may occur at any age. Most of the cases reported in the European literature occurred in infants and children. The clinical picture of acute aseptic meningitis has been ably described by Wallgren,[2] Gunther,[4] Viets and Watts,[15] Armstrong and Dickens.[12] The onset of the

*We are indebted to Dr. Hollis Johnson for permission to report this case, which occurred in his private practice.

illness is usually sudden, and is indicated by the development of chilly sensations, headache, drowsiness and fever. Soon nausea and vomiting and stiffness of the neck develop. The patient appears critically ill at the onset and usually exhibits cervical rigidity, Kernig's sign and hyperactive reflexes. The headache is severe and is out of proportion to all other symptoms, but loss of consciousness rarely supervenes. Except for edema of the optic disc in an occasional case there is no cranial nerve involvement. The pulse rate is proportional to the height of the temperature, but in some instances there may be a bradycardia.

In the great majority of cases fever is present at the onset, is intermittent in character, and declines by lysis. The average height of the temperature is 101° F., although it has been found to be as high as 104° F. The duration of the fever is said to vary from one to three weeks although in two of our cases it was present for only 3 days. In one case reported by Viet and Watts[15] fever persisted for 75 days.

The leukocyte count in the recorded cases varies between 4,000 and 13,000 per cu. mm. of blood, with an average of about 10,000 per cu. mm.

The cerebrospinal fluid examinations are of the greatest diagnostic importance. The pressure of the fluid is either normal or but slightly increased. The cell count varies considerably, the average in the reported cases being about 400 per cu. mm. with extremes of 40 and 3,000. In our three cases the count did not exceed 303 per cu. mm. The cells are predominantly lymphocytic in type, although early in the disease a high percentage of polymorphonuclear cells may be present. The spinal fluid total chloride content is normal as is the sugar in the reported cases. Two of our cases had spinal sugar values of 39 and 40 mg. per 100 c. c. The protein content of the fluid is slightly increased. Pellicle formation does not occur. There are no demonstrable organisms in the fluid on microscopic examination and cultures of the fluid remain sterile.

The diagnosis of acute aseptic meningitis is made by a process of exclusion. Although the history and neurological findings in this condition are impressive and conform to a definite clinical pattern the fact remains that practically any disease which is associated with or productive of meningeal irritation may at sometime in its course produce a similar picture. With this in mind one must always consider the possibility of cerebrospinal fever, septic meningitis due to a variety of organisms, tuberculous meningitis, and syphilitic meningitis. The examination of the cerebrospinal fluid will in most instances clarify the situation. Meningismus in association with typhoid fever, scarlet fever, measles and mumps must be excluded. The meningeal manifestations of either poliomyelitis or epidemic encephalitis may for a time mask the true nature of these infections and lead to diagnostic errors. Unfortunately the cerebrospinal fluid examinations here would be of but little help in making a proper differentiation. In the vast majority of cases, however, subsequent developments would rapidly reveal the true nature of these diseases.

As has been indicated the prognosis in acute aseptic meningitis is excellent. Indeed one is led to question the diagnosis in the few reported instances in which sequelae occurred (encephalitis, Anderson and Wolff;[3] strabismus, Eckstein;[6] changes in personality, Gunther[4]).

ETIOLOGY

Although the etiology of acute aseptic meningitis is not known, extremely important contributions to our knowledge of the subject have been made in recent months. Prior to 1934 theories had been advanced relating the condition to virus infections, emphasis being placed upon a possible etiological relationship to poliomyelitis and encephalitis.

In 1934, Armstrong and Lillie[13] encountered a filterable virus in the course of transmission experiments in monkeys previously injected with autopsy material from a case of encephalitis, but were uncertain whether or not the infectious agent had originated independently in the animals or was derived from the autopsy material. This virus produced a choriomeningitis in monkeys and mice. Armstrong and Wooley[16] reported further work with this virus in 1935. They isolated two additional strains of viruses; one from an atypical case of encephalitis, and one from a monkey inoculated with poliomyelitis virus. All three strains produced a similar pathological picture in experimental animals and apparently were identical immunologically. It was therefore assumed by Armstrong and Wooley that these three strains were identical and constituted a single virus entity. These investigators showed, moreover, that serum collected from a person eleven months after an attack of aseptic meningitis protected mice against this virus.

Traub[17] in 1935 isolated a virus from apparently healthy white mice. This virus was originally activated by the injection of boullion intracerebrally into mice and after animal passage became capable of producing choriomeningitis in mice, guinea-pigs, and monkeys.

Rivers and Scott[14] were the first to isolate a virus from the cerebrospinal fluid in human cases of aseptic meningitis. This was done in two instances. These workers were able to reproduce a choriomeningitis in white mice, guinea-pigs and monkeys. Rabbits were not susceptible.

In June of 1935 Armstrong and Dickens[12] reported that they had interchanged animals and sera with Rivers and Traub and had found that immunologically the several viruses were identical. They stated moreover that serum from four patients with acute aseptic meningitis who had recovered from the disease protected mice against the several viruses. In one instance the serum of a patient early in the course of the disease did not protect from the virus but serum obtained two months after the illness did protect. Armstrong and Dickens therefore suggested that acute aseptic meningitis really constitutes a new disease entity and favored the use of the designation "benign lymphocytic choriomeningitis."

Attempts were made to transmit the disease to monkeys and mice with cerebrospinal fluid (3 instances) and nasopharyngeal washings (1 instance) obtained from our three patients with acute aseptic meningitis. None of the animals injected with the original material obtained from patients developed evidence of virus infection. No attempt was made to carry the experiment beyond the first animal passage, that is, passage of the material through a second or third series of animals was not done. Blood serum was obtained from our three patients approximately two months after recovery and forwarded to Dr. Thomas M. Rivers who found that the serum did not neutralize the virus isolated by Rivers and Scott in 1935. Dr. L. T. Webster found that the sera did not neutralize the virus isolated by him from the recent St. Louis epidemic of encephalitis.

SUMMARY AND CONCLUSIONS

Three instances of acute aseptic meningitis are reported. The disease is characterized by the abrupt onset of relatively mild meningeal manifestations, a benign course terminating in complete recovery without sequelae, and by certain alterations of the cerebrospinal fluid. Important diagnostic and etiologic considerations are discussed.

Our experience suggests that if a virus is the etiological factor in this disease it is not always recoverable by the methods employed. The inability of convalescent sera from our cases to protect animals against infection with the Rivers virus suggests that if virus infection is the cause of the disease the viruses involved are not always immunologically identical.

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DISCUSSION (*Abstract*)

Dr. Thomas M. Rivers, New York, N. Y.—The paper of Drs. Riven and Fleming raises the question of whether "acute aseptic meningitis" represents only one disease. When we first encountered the virus of lymphocytic choriomeningitis in the spinal fluid of two patients, we were inclined to believe that we had found the etiological agent of acute aseptic meningitis, but further work clearly showed that many cases with the clinical picture of acute aseptic meningitis were not caused by our new virus.

The fact just mentioned did not disturb us, because the tissues of the body, and this is particularly true of the central nervous system, are capable of reacting to injury in a limited number of ways. Consequently, different viruses affecting the central nervous system may produce similar or identical clinical pictures. Such a statement is also applicable to bacterial infections of the meninges, because without bacteriological and microscopical examinations of the spinal fluid, it

would be impossible to distinguish one purulent meningitis from another. Now we believe that acute aseptic meningitis is not a disease entity caused by one filterable virus, but that it represents a group of diseases with similar clinical pictures which are induced by several viruses, one of which is the virus of lymphocytic choriomeningitis.

SEPTIC INFECTIONS OF THE LEPTOMENINGES*

By FREDERICK C. SCHREIBER, M.D., F.A.C.S.
Washington, District of Columbia

The controversy surrounding the cerebrospinal fluid, its physiology, pathology and therapy in disease, is apparent to all of us. No subject matter of medicine brooks more contention and enjoys less unanimity of opinion than septic invasion of the leptomeninges. I am sure this statement will rouse no controversy and it is largely because of the great diversity and disparity of opinions surrounding this subject that this paper is presented. We shall confine ourselves largely to a discussion of controversial factors and for this reason shall omit matters which are agreed upon, such as the modus operandi of infection, the types of infectious organisms and the surgical procedures which must be instituted for cure.

It is necessary that we define the lesions falling within this field. The term, septic leptomeningitis, presumes that the leptomeninges have been invaded by suppurative organisms and that they have been recovered in the cerebrospinal fluid through the medium of spinal or cisternal taps and have been accompanied by physical, chemical and cytological changes indicative of this lesion. We do not propose to concern ourselves with incipient manifestations in which there appears a relative pleocytosis without recovery of organisms either in smear or culture. These conditions called serous or sympathetic meningitis may or may not be the beginning of a diffuse suppurative invasion.

Our present conception of the cerebrospinal fluid is founded upon investigations dating back to Galen, Vesalius and Valsalva. Some seventeen centuries later, Magendie[1] (1842), in an outstanding monograph, described the ventricular and subarachnoid systems, stating that they were continuous and one. In 1854, Faivre[2] described the choroid plexus and speculated upon its secretory activity. Retzius[3] and Quincke,[4] in 1870 and 1872, respectively, concluded that the cerebrospinal fluid was absorbed through the Pacchionian corpuscles of the superior and lateral venous sinuses. Weed,[5] in 1914, concluded that the cerebrospinal fluid was liberated not only by or through the choroid plexus, but that it found its escape through the perivascular spaces into the subarachnoid area. These various facts occasioned further investigation as to the origin of the cerebrospinal fluid. Luschka[6] championed the idea of the secretory activity of the choroid plexus which was suggested previously by Faivre. Generally this theory was unchallenged until Metrezat,[7] in 1912, published his work dealing largely with the chemistry of the fluid, but definitely concluding that the choroidal plexus acted as a dialyzing membrane. He stated that a perfect osmotic equilibrium existed between the blood plasma and the cerebrospinal fluid. He determined the fact that the fluid protein is less than the blood plasma protein and that the chlorides of the fluid in the form of sodium chloride are in greater concentration in the cerebrospinal fluid than in the blood plasma. Although Retzius and Quincke had intimated the manner of the fluid absorption, it remained for Halliburton[8] and Weed to establish the fact that the pressure of the cerebrospinal fluid is greater than the pressure within the venous sinuses, and that the rate of absorption is dependent upon the disproportion of these two pressures. Their experiments further established the fact that the rate of absorption could be augmented by increasing the osmotic pressure of the blood, and that hypertonic solutions injected intravenously caused a greater rate of absorption. Conversely, hypotonic solutions injected intravenously produced hydration of the perivascular spaces of the brain and the cord, occasioning widening of the perivascular pathways. Upon the establishment of these facts Hampton,[9] of England, and Kubie,[10] of America, based the rationale of their theory of forced cerebrospinal drainage.

It has been definitely determined that there is direction to the flow and movement of the fluid. The escape of choroidal fluid through the various ventricles to the cisterna magna is known, but it remained long a matter of conjecture what direction it assumed from here. It is now held that from this point the fluid courses over the cerebral hemisphere towards the greater venous systems, where it is absorbed.

*Read in Section on Ophthalmology and Otolaryngology, Southern Medical Association, Twenty-Ninth Annual Meeting, St. Louis, Missouri, November 19-22, 1935.

This movement described as a mass movement is affected by variations of pressure occasioned by pulse and respiration. Starling's[11] excellent work intimates the cranial course, but does not regard the caudal circulation. In fact, one is allowed to speculate for himself concerning this. Flexner's[12] experiments on animals are illuminating and not without practical clinical application. He finds that sufficient fluid is formed in the lateral ventricles of the etherized cat to renew their total volume 17 times in 24 hours, and that the fluid of the third ventricle is changed 60 times in 24 hours, in the fourth ventricle 75 times, while in the subarachnoid space the fluid is changed between four and five times. It appears, then, that the greater the volume the less the fluid movement and that in the basal cisterna almost a stasis exists. This would lead one to speculate upon the reason for the malignancy of infections directly introduced into the cisternal spaces.

The exhaustive researches of Mestrezat in determining the chemical structure of the cerebrospinal fluid and the disproportion between its components and those of the blood stream have been verified by Fremont-Smith,[13] Loeb and Palmer[14] and McLean.[15] Of more immediate and vital interest is Kolmer's[16] work, which determined the absence of specific antibodies in the cerebrospinal fluid as opposed to their presence in the blood plasma of a large majority of human beings. Because of this he reasons the fluid to be particularly vulnerable to infection. He has demonstrated the presence of antibodies against streptococcus, pneumococcus and staphylococcus in the blood plasma, but has failed to determine their presence in the cerebrospinal fluid. Furthermore, he has noted the absence of any complement which might be found in the blood plasma. He has definitely shown the presence of antitoxic antibodies in the blood stream against tetanus and yet failed to demonstrate their presence in the fluid.

Because of this, Kolmer and his associates have attempted to immunize against the pneumococcus and streptococcus in contemplated sinus and ear operations. Kolmer seems convinced of the impossibility of passing over antibodies into the spinal fluid in normal persons, but feels that there may be some alteration of the selective barrier which the choroid plexus manifests during meningeal irritation. His experiments with Type I pneumococci have been somewhat convincing, but other invading organisms have not been deterred in their action by preventive inoculations. He recommends the use of autogenous vaccines in chronic sinus and ear infections, especially ethmoiditis, before operation when meningitis is feared. This form of immunologic therapy has been questioned by Neal, Jackson and Applebaum,[17] who contend that its efficacy would be open to question as meningitis is a relatively infrequent complication of sinus and ear surgery. Furthermore, they allude to the time that would be required to vaccinate against infection and the possibility of sensitizing the patient. There is reason to believe that these experiments will be elaborated upon and that some technic may yet be achieved by which a higher threshold of immunity to infection may be established.

The successful conduct of any septic invasion of the leptomeninges depends directly upon early diagnosis and immediate action. Where formerly spinal taps were diagnostically open to question of expediency and judgment, now it is universally held that this procedure not only permits detection and early diagnosis, but gives other evidence of great importance. Kolmer[18] has requested early and frequent taps and overruled any objection to this procedure. He realized that temporization in dealing with these entities was a serious matter and that if any hope were entertained for ultimate cure, treatment must be instituted early. Kopetzky,[19] who recognized the necessity of early diagnosis, said:

> "The finding of the bacterial invaders in the cerebrospinal fluid comes too late to permit diagnosis at the stage of the invasion when therapy is effective."

He proposes a diagnostic scheme based upon chemical changes relating to the reduction in the sodium chloride and bicarbonate and increase in the lactic acid content of the fluid. It would appear that the work from which these conclusions were drawn was excellently done, yet one must reserve his opinion regarding the expediency of operating upon the evidence of these changes alone. Recent experimental work discloses an alteration downwards in the sodium chloride content of the fluid when the dura of the posterior fossa is exposed.

The diagnosis of meningitis is determined by clinical as well as laboratory evidence. Indeed, the diagnosis of meningitis by laboratory methods alone may be quite misleading. One must not be misled if organisms are not recovered by lumbar puncture, and, perhaps, only slight cellular disturbance is noted. Eagleton[20] and others have drawn attention to this apparent misleading evidence. Eagleton says:

"Suppurative meningitis is not necessarily associated with high cell count and with organisms in the fluid from the lumbar region. Jenkins has demonstrated that micro-organisms in the cranial subarachnoid spaces may be associated with clear sterile fluid with a cell count of but 48 from the lumbar region, and I have obtained sterile fluid from the basal cisterna while the fluid from the lumbar region contained bacteria. Consequently, we should wait for the presence of micro-organisms or high cell count before making a diagnosis."

Thus it is that collateral help may be misleading rather than informative. It recalls sharply to mind the necessity for careful evaluation of all phenomena surrounding any given case and the fact that here, as with other laboratory aid, one must be conscious that a negative laboratory finding does not establish beyond peradventure a negative clinical condition.

However, negative fluid findings are the exception rather than the rule. Spinal puncture affords the opportunity of early and absolute diagnosis and is a measure of prognostic importance as well. Greenfield[21] suggests manometric findings before any fluid is withdrawn. He further counsels against the loss of too great an amount of fluid and states that under no circumstance should an amount be withdrawn sufficient to allow the manometric reading to fall below two-thirds of the original reading. This is of practical clinical importance and fortifies against the possibility of cerebral edema from sudden and precipitate reduction in pressure and mitigates against brain stem herniation into the foramen magnum. Increased pressure findings with slight or marked turbidity suggest disease. Chemical study of the fluid with the disclosure of the reduction of the sodium chloride content, increase in albumin and decrease or absence of glucose definitely suggests bacterial invasion. These changes, coupled with positive cultural findings, establish the diagnosis of septic leptomeningitis beyond qualification.

The symptoms are those of a general toxemia with well defined manifestations related to the cerebrospinal axis. The latter are the most diagnostic and depend upon toxic and pressure phenomena. Layton[22] has attempted to prove that cervical rigidity is the earliest symptom accompanying cerebral invasion secondary to acute mastoiditis. He regards Kernig's sign a later phenomena and feels that it implies extension of the suppuration to the area of the lumbar cord. His contemporaries do not fully agree with his findings regarding cervical rigidity, and Symonds[23] has stated that he found it entirely absent throughout the course of meningeal states. He contends that cervical rigidity is present when the suppurative invasion involves the meninges dorsal to the medulla. The classical picture of sudden invasion within the calvarium suggested by deep, agonizing headache, associated with vomiting, fever, chills, spasticity of the neck with positive Kernig sign point strongly to meningeal invasion. There are some paradoxes, however, in its symptomatology: the pupillary reflexes are present in the early stages and absent later, the knee reflexes may be exaggerated first, but are later absent, and whereas the patient denotes apprehension and is restless at first, later he becomes drowsy with delirium and coma, the terminal symptoms.

Eagleton[24] has summarized the important diagnostic features surrounding this lesion. He speaks of the duration of the meningeal manifestation, its probable source of origin, and its type. He stresses the chronological sequence of symptoms and their duration, discusses the advisability of neurological examination in which the acoustic and vestibular mechanisms of the ears are interrogated, the field forms taken and the fundus of the eyes examined. Likewise the spinal fluid is investigated, the pressure noted, physical qualities recorded, and cells and micro-organisms determined. All cases should have frequent blood cultures, the number of cultures being determined by the clinical course of the disease. Neal also favors the repeated examination of the blood stream for detection of invasion, and all agree that blood stream infection is universally fatal. Again a thorough study should be made of the mastoid and petrous portion of the temporal bone and one must not fail to submit the accessory sinuses to thorough clinical and x-ray study. Eagleton differentiates between sphenoidal and mastoid invasion and states that most pneumococcic Type III meningitides are secondary to sphenoidal invasion and that the pial vessels are thrombosed. These studies should lead to a definition of the portal or portals of invasion. However, the immediate focus may be difficult to determine, particularly when there are changes related to both the accessory sinuses and the ears.

In purulent meningitis immediate intervention is necessary. Suppurative meningitis parallels to a degree meningococcic meningitis in which Worster-Drought and Kennedy report five cases treated on the first day with the survival of every patient; among 24 treated on the second day the mortality was 21 per cent, and of

20 cases treated on the third day, 55 per cent died.

A search of the literature discloses 110 recovered cases of septic meningitis. Rosenburg and Nottley[25] reviewed 41 cases and were amazed that in this series 29 proved to be of otitic origin. In this series spinal taps were used frequently, and antistreptococcic serum was injected into the spinal canal as well as intravenously. A study of the therapeutic measures instituted in cases which recovered shows the employment of every conceivable method. The striking feature is the lack of unanimity of opinion as to therapy. In his summary of these cases, Applebaum[26] says:

"In view of the variety of methods employed it is difficult to attribute the successful outcome in any of the recovered cases to a specific form of therapy. There does not seem to be sufficient evidence in favor of extensive or radical operative procedure."

Neal says:

"It would seem from our own experience and from a study of the literature that the most important therapeutic factor, aside from the removal of the primary focus of infection, is adequate drainage of the cerebrospinal fluid. Unless there is blocking, this can be accomplished by lumbar puncture. There is no evidence that the more radical forms of drainage are more effective. A greater number of recoveries has followed ordinary spinal drainage than any other form of treatment."

Any therapy directed against the progress of this disease must undertake the immediate and eventual control of the factors pertinent to the ultimate recovery of the host. The underlying influence naturally resolves itself about the presence of specific types of organisms which have invaded a fixed tissue space. Proliferation and growth of the invaders has perverted the function of the cerebrospinal fluid, increased the total quantity, and established toxic substances which exert a deleterious and often fatal effect upon the host. The immediate object of therapy must very obviously be directed towards the annihilation of the invading organisms. Establishment of a more normal ratio between those factors which create intracranial balance as dictated in the Monroe-Kellie doctrine is of slightly less importance. The removal of toxic products of bacterial and cell metabolism is another important feature. All of these must be reckoned with in instituting any type of therapy.

There are two schools of therapy concerning septic invasions. One advocates the introduction into the cerebrospinal axis of antisera and many chemical agents. This work has been outlined and sponsored by Kolmer. His results with pneumococcic antisera have been recorded, and experiments upon animals have proven that Type I pneumococcus is more readily amenable to therapy than others, and that Felton's antipneumococcic serum has many antibodies directed against this type of organism. The results with pneumococcic infections, because of a rapid agglutinative method of typing, bid fair to aid materially in favorable end results in this infection. The results of bacterial investigations in which Type IV pneumococcus has been further divided into definite groupings presents a clearer conception of these organisms than was formerly possible. In fact, recent results in suppurative meningitis due to the pneumococcus have proven the efficiency of Felton's serum in Types I, II, VII, XII, XIV and XVIII. In Types III and the so-called heterologous groups of pneumococci, Felton's serum has slight if any effect. In these cases a polyvalent serum may be used, but there is some evidence that a nonspecific serum such as the antimeningococcic serum injected early in these cases exerts a favorable influence. Under any circumstance, the determination of the agglutinative type of pneumococcus may be consummated quickly and this fact mitigates against delay in the proper institution of specific antiserum treatment. This is particularly important, inasmuch as pneumococcic meningitis is a most fulminating infection and is associated with the early formation of plastic exudate which tends to defeat therapy.

Successful typing of the streptococcus is not yet upon a satisfactory basis. The hemolytic streptococcus is the most frequent invader, but there is little that one may determine about its agglutinative types. Williams[27] states that in a series of 37 streptococcic cases studied by Neal and Gosling, they were able to isolate 2 into their largest scarlet fever group (Type Sub 1), 1 into a scarlet fever group, Type IV, 2 into an erysipelas type group, and a group of 7 which forms a new agglutinative group. These collaborators regard the streptococci as particularly virulent, as they produce two types of toxic bodies, the one excreted during their growth and proliferation, called exotoxin, and the other existing within the organism, called endotoxin. They say that in the future they shall attempt the creation of antibodies directed against the endotoxin itself, a type of specific therapy which would remove the invader. They report the successful use of antiscarletinal serum in

two cases and feel that their results were due to the specific antiserum used.

For some time it has seemed apparent that specific antisera employed early might be of inestimable worth. A case of pneumococcus meningitis occurring in the practice of one of my contemporaries, in which autogenous serum was used, recovered. Fifteen c. c. of blood serum obtained from the patient introduced into the spinal canal produced some anaphylaxis, but was otherwise well withstood. This case was a Type IV pneumococcus meningitis in which polyvalent antipneumococcic serum was introduced into the spinal canal as well as given intravenously. Baum[28] has recently recorded the use in streptococcic infections of specific human serums secured from recent streptococcic cases. Specificity is determined by the ability of the serum to agglutinate organisms harbored by the patient. It seems evident that we shall at some time secure donors whose blood is not only correctly typed to the recipient, but whose serum contains definite and specific antibodies required to combat the infection at hand.

The other school proposes forced spinal drainage and is sponsored by Kubie. His method is a matter of record and has been used by others, particularly Fremont-Smith and Retan.[29] Fremont-Smith and coworkers use a modification of the Kubie method, draining the lumbar sac from four to six hours. From 500 to 1,000 c. c. of water is given by mouth per hour. Diuresis is delayed by the injection of pitressin 0.5 c. c. Retan remarks that this method may reduce the osmotic pressure of the blood to some slight extent, but he feels that the introduction intravenously of a hyptonic saline solution is essential if the perivascular spaces are to be forcibly washed out. This form of treatment must be instituted early, particularly in those cases in which the pneumococcus or the influenza bacillus is the invader. He stresses the necessity of recovering the organism by direct smear; for otherwise one may be dealing with an aseptic meningitis or an abscess contiguous to the dura. His recent contribution in which he gives the results of treatment of 12 cases of septic meningitis proves rather conclusively that in these lesions perhaps little is to be afforded by his method. Theoretically the method has some compelling attributes; practically it is difficult to reconcile oneself to it.

Reference to drainage of the infected theca through spinal taps has not been spoken of, although of course it has been implied. The majority of successful end results have followed this procedure rather than the more radical and formidable ones. It has been said that in infectious states of the meninges the amount of cerebrospinal fluid escaping into the subarachnoid space approximates slightly over one liter in 24 hours. The urgency for relief from the pressure of this increased volume of fluid is apparent. It has always seemed to me that the removal of any given quantity of fluid shows lack of judgment and understanding. The quantity removed at any given time must be governed by the manometric reading at the beginning of the operation and the pressure must never be dropped below two-thirds of the original pressure. Mounting pressure and increase in the cell count of the fluid are indications for more frequent intervention than a stationary or receding picture would occasion. Limitation of fluids by mouth to 1,000 c. c. or less in 24 hours should be complementary in lessening the total fluid volume in the cerebrospinal axis.

In closing, it is urged that specific antisera be employed early when opportunity affords. As an alternative, auto or iso-serum from the infected individual may be transposed to the spinal canal as a therapeutic measure. It contains antibodies which cannot gain entrance into the cerebrospinal axis in any other way.

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DISCUSSION (*Abstract*)

Dr. John H. Foster, Houston, Tex.—For years we, as otolaryngologists, were forced to a hopeless view of purulent meningitis. Today some light seems to be breaking. The sum total of the work and observations of various workers is a step forward. Notable work is being done by the Committees on Meningitis of the New York Otological Society and the American Otological Society in setting certain definite standards as to what constitutes generalized purulent meningitis and in making an effort to check the results of the various lines of treatment.

At present I have certain definite convictions in regard to purulent meningitis:

(1) We know of nothing that influences favorably certain fulminating types of cases. It is almost unbelievable that we can ever hope to accomplish a cure in these.

(2) A large number of cases are, for a considerable length of time, localized and, if recognized during this period, may be prevented from becoming generalized. Early spinal puncture in every suspicious case is essential to an early diagnosis. Means contributing to the prevention of localized meningitis from becoming general include: (a) thorough removal of infected foci; (b) wide decompression; and (c) drainage of the infected area, if possible.

(3) The work of Kolmer, corroborated by the experience of others, notably Ersner and Mendell, gives us reason to believe intra-carotid medication may influence infection in the meninges.

(4) Certain vaccines and serums may be of benefit.

(5) Forced spinal drainage, as devised and described by Kubie and Retan, is, in my opinion, one of the greatest steps forward in the treatment of cerebrospinal diseases. Time does not permit a discussion of this procedure at length.

We are all familiar with the temporary benefit of spinal puncture in meningitis. Often a case will seem to do well on this alone for days. Usually the drainage lessens day by day and finally we are able to get no return flow. With the forced drainage the flow keeps up, pressure is relieved and I believe we may hope that the formation of the large masses of plastic exudate over the surface of the brain may be prevented.

Again Retan has shown that cases of cerebrospinal syphilis do particularly well when the administration of antiluetic drugs is carried on in conjunction with forced spinal drainage. The assumption is that the passage of the drugs from the blood stream to the cerebrospinal fluid is facilitated by this method. It is reasonable to believe that other drugs and serums may be used in like manner in cases of meningitis.

Within the past year I have had one case presenting the classical signs and symptoms of otitic meningitis in which forced spinal drainage was used for twenty-six days with a most satisfactory result in the prompt control of severe symptoms and ultimate complete recovery. This case will be reported in detail later.

Dr. Millard F. Arbuckle, St. Louis, Mo.—Progress of course has been made in the treatment of infections of the meninges, but much greater progress will be made if we all remember to obtain more accurate bacteriological studies in each individual early in the case and to report our results. It is not essential that a man have a large series of cases in order to render important service by reporting them. As an example of this fact it will be recalled that O'Dwyer, in reporting his study of laryngeal diphtheria and the perfection of intubation, reported at first only one successful case. Later of course he reported many. The same spirit should govern us in this disease. I have had several cases in which I am firmly convinced that infectious meningitis was present, but for lack of some minute detail the value of the report of the case is decreased.

CLINICAL DEDUCTIONS FROM CYTOLOGICAL FINDINGS OF THE NASAL SECRETIONS*

By JOHN R. HUME, M.D.
New Orleans, Louisiana

It is the purpose of this paper to present the rationale and draw conclusions from the studies of ourselves and others regarding the value of the nasal smear to the clinician in otolaryngology.

We find among the various inflammatory phenomena, when the nasal and sinus mucosa are subjected to irritation, the exudation of certain of the blood cells into the subepithelial layer; especially is this noted in the perivascular spaces.

The cells find their way through the impaired or even destroyed surface epithelial layer and appear in the secretion. By a study of the cells contained in this secretion, we are able to draw conclusions as to the probable pathologic changes in the mucosa and judge something as to the nature of the irritant.

Nasal secretions taken from the normal nose contain few cells. If taken from one with pathologic changes the cells are numerous.

*Read in Section on Ophthalmology and Otolaryngology, Southern Medical Association, Twenty-Ninth Annual Meeting, St. Louis, Missouri, November 19-22, 1935.

The exudative white cells that appear in the nasal secretions as a result of pathologic changes occurring in the mucosa are the neutrophils, small and large monocytes and eosinophils. While the plasma cell is often noted in tissues, they are rarely found in the nasal secretions. The red cells or erythrocytes appear only in very intensive congestion and may thus escape from the vessels or come from rhexis of the small vessels.

The polymorphoneutrophils are the cells of acute inflammation. They are actively ameboid and phagocytic. Their function is the destruction of living bacteria by phagocytosis, carried out especially in conjunction with the opsonins of the blood serum.

The small mononuclear and lymphocyte may be present in the later stages of an acute inflammation. In chronic inflammation it assumes a position of commanding importance. It appears to accomplish its work by antitoxic rather than by phagocytic activity.

The large mononuclears are endothelial cells, having great phagocytic power. They carry away in the lymph stream the dead bodies of leukocytes, bacteria and tissue cells. Present in small numbers during the early stages of an inflammation, they obviously become much more numerous in later stages. All in all they may be considered as reparatory scavengers and include the large group of reticulo-endothelium, histiocytes and macrophages.

The eosinophils appear in all conditions in which anaphylaxis plays a part. The origin and function of the cell is unsettled. Eosinophil cells are not of uniform type. Many cells have coarse granules and are bilobed; others are mononuclear and have much finer granules. While this cell type has been strongly linked with allergic conditions, it must be noted that it frequently appears in subacute and chronic states in various structures having mucous membranes, especialy in appendicitis, cholangeitis and salpingitis.

Assuming that these cells filter into the secretions from the tissue at the location of the pathologic process, they must be removed along lines of greatest ciliary action. Hilding has shown that this action is greatest in the meatuses.

Since the anterior group of sinuses drain into the middle meatus, this would seem to be the location of choice to secure material for cytologic studies of these areas. It is obvious that the olfactory fissure and region of the sphenoidal ostium would furnish satisfactory material for studies of the posterior cell group. When stagnation, due to ciliary inhibition or destruction within a sinus exists, the diagnostic value of this material would be minimized. Proetz observes, however,

> "In twenty-two specimens removed at operation, some of them from sinuses with the worst imaginable chronic infections, the cilia were beating vigorously and to all appearances normally in every case, with one single exception."

With such established or accepted premises, it can be deduced that properly procured material should form a justifiable basis as to the nature of the existant lesion with which we have to deal. Perhaps erroneous conclusions may be deduced from a prevalence of eosinophils unless other confirmatory criteria are reviewed in the analysis of the case.

It is agreed by all investigators of the problem of allergy that the eosinophil is at some time noted in large numbers during an attack. During the quiescent period, while usually found, they are in greatly reduced numbers. If, however, the symptoms are very severe, the secretions become very profuse and are often acellular. It has been also observed that the ratio of eosinophils to neutrophils is definitely lowered in the presence of superimposed infection.

Lindsey and Walsh state that the eosinophil found in the secretion is indicative of vasomotor rhinitis. No allergy was demonstrated in 14 per cent of cases in which there was a high percentage of eosinophils in the nasal secretion. They also conclude that routine examination of smears affords a simple and effective laboratory aid in the diagnosis of vasomotor rhinitis when the clinical signs of the condition are marked by those of a complicating infection.

Johnston and Goldstein, in the study of 34 cases suspected of being allergic, agree in the main with the findings of Lindsey and Walsh as regards the significance of the eosinophil. The latter found few lymphocytes in their smears, however, which was contrary to the findings of Johnston and Goldstein, who found a high per cent of those cells present in many of their smears.

Brown, in discussing the eosinophil in allergy, disagrees with the opinion that the eosinophil in asthma and hay fever is practically diagnostic of protein sensitization and cites studies to support his contention.

Sewell and Hunnicutt have made extensive cytological studies of the sinus secretions and have demonstrated their value as a diagnostic measure. Their work being studies of cases of acute and chronic sinusitis, deals more especially with the significance of the monocytes and the polymorphoneutrophils. They conclude that the polymorphoneutrophil leukocytes found in the sinus secretions are evidence of infection; if they persist in spite of treatment, one is dealing with chronic sinusitis; the presence of mononuclear leukocytes, a low-grade inflammation that is undergoing resolution.

Sewell found in 98 sphenoids examined only two eosinophils in the series. Acknowledging that some may have been overlooked, he says:

"The fact remains that the number is small if we are to believe that they commonly accompany the discharge associated with allergic disease and if we agree to the unsubstantiated assumption that allergy is the only cause of sinusitis."

Our studies are made on 150 routine nasal and sinus cases. The smears for study were taken with a small cotton tipped applicator from the middle meatus and olfactory fissure. In each instance slides were prepared from both nostrils.

In one hundred and forty-four cases the same type of cell was found in preponderance in both nostrils. In six cases they differed. Neutrophils prevailed in 10 per cent of cases; eosinophils in 15 per cent; large monocytes in 14 per cent, and the small lymphocytes in 60 per cent. In 48.6 per cent the eosinophils appeared in numbers greater than 5 per cent; the neutrophils and lymphocytes were found in approximately equal numbers in 5.4 per cent; the neutrophils and eosinophils in 2 per cent, and the eosinophils and lymphocytes in 5.4 per cent.

In twenty-seven instances the large monocyte was noted in great numbers where the small monocyte was in preponderance. In four cases the same condition was found with the neutrophil. In six cases an entirely different cell picture was observed from the two nostrils.

An observation that might suggest further study was that in smears containing more than 75 per cent of lymphocytes, bacteria were seen in more than the usual number.

In the cases studied the nasal smears suggested the existant pathologic condition present in 86 per cent as indicated by routine examination, sinus lavage and x-ray studies. Repeated smears as suggested by Johnston and Goldstein would probably have yielded better results.

In connection with our cytological and clinical studies of rhino-sinusitis we conclude:

(1) That the polymorphoneutrophils present in the nasal secretions indicate an acute inflammatory reaction.

(2) That the lymphocytes present in the nasal secretions indicate chronic inflammation with round cell infiltration of the subepithelial layers.

(3) That the eosinophils present in the nasal secretions in numbers greater than 5 per cent suggest a hypersensitivity, and proper tests should be made before surgical procedures are instituted other than for the purpose of ventilation and drainage. We are not convinced, however, that the eosinophil is present only where an allergic background is existant. Its origin and function must be better understood before its exact relation to allergy is established in fact.

(4) Presence of the large monocytes in the nasal secretions should be considered as a favorable omen; it indicates that a maximum reparative effort is being made cytologically to combat the pathological processes.

(5) Polymorphoneutrophils or lymphocytes present, in conjunction with eosinophils, would at least suggest a bacterial invasion on an allergic background.

(6) The study of the nasal smear should be instituted as a routine measure. With a reasonable degree of accuracy and by a simple procedure we are able to determine whether we are dealing with an acute inflammation, a chronic process or a possible allergy or an allergy complicated by infection.

(7) Smears examined during the treatment of a case will afford information as to the progress being made.

(8) It does not seem improbable after many thousand nasal smears have been examined and correlated with the physical and pathological findings that it will assume the importance as a diagnostic measure that the differential white cell count holds in general infections.

I wish to express my appreciation to Dr. H. J. Shattenberg, of the Department of Pathology of Tulane University, for his kindness in preparing the lantern slides.

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DISCUSSION (*Abstract*)

Dr. I. S. Kahn, San Antonio, Tex.—There are several points of interest in this subject. First is the fact that the test is admittedly not infallible. Certainly eosinophilia is not present during the quiescent stage of an allergic rhinitis and not during the initial extremely watery discharge of an acute severe case where the diagnosis is obvious by other measures. However, repetitions of the search for eosinophils will reveal the presence of these cells in abundance at some time in every allergic rhinitis case. Whether the presence of these cells in abundance is an invariable definite diagnostic sign of allergy is not known.

An excellent method of collecting the discharge for examination is by the use of a cellophane handkerchief at the time there is a natural normal desire to evacuate the secretions by blowing the nose. Forcible commanded blowing gives poor results. Material collected in this manner and sealed in a jar will often be suitable for examination at the end of two or three hours. This gives a means for determining the allergic basis of cases with early morning symptoms that clear during the day, direct examinations of which at that symptom time are impractical.

To the allergy worker this test is valuable in determining the presence of coincident or transient complicating infections which may require local treatments by a consultant.

Dr. C. C. Swann, Asheville, N. C.—Dr. Hume has presented us with practical, quick diagnostic aid in determining the presence of the products of inflammation in the nasal secretions. It is noteworthy that many of his patients showed no significant pathological changes, either to inspection or x-rays, and principally by cytologic study was it determined that active disease was present.

I believe that most of us are prone to dismiss those patients who present a fairly normal looking mucous membrane and practically negative radiograph. Conversely, many sinuses showing thickened lining membranes and hyperplastic changes in skiagraphs, which are subjected to surgery, are dormant so far as active disease is concerned, and would prove essentially negative to cytologic investigations.

It has not proven practical for me to do cytologic washings on the individual sinuses in routine examinations, though this has been done in selected cases. It does seem feasible to take a quick slide from the middle meatus and sphenoethmoidal and olfactory fissures in all suspected cases and later, if desired, do cytologic washings on the individual sinuses of positive cases.

Heretofore I have had no guide, other than cytologic washings in selecting cases for autogenous vaccine. Since the specific antigen is usually given to those patients presenting intractable, chronic symptoms, we should expect beneficial results from this therapy when there is present a heavy bacterial flora and high percentage of lymphocytes.

I believe that about one-fourth of my sinus patients have an underlying allergic factor, and in these cases I avoid surgical procedures when it is possible to do so. Routine cytologic studies of smears will certainly aid us in arriving at the etiology and the proper course to follow in caring for the individual cases.

TREATMENT OF FRACTURES OF THE TIBIA AND FIBULA BY MEANS OF THE ROGER ANDERSON SPLINT*

By O. B. Bolibaugh, M.D.
Washington, District of Columbia

The purpose of this paper is to report our experience at Walter Reed General Hospital in the treatment of fractures of shafts of the tibia and fibula by means of the Roger Anderson splint.

During the past eighteen months we have treated thirty fractures of the tibia and fibula. Twenty-three of them have been reduced by means of the Roger Anderson splint. Fourteen of our cases were members of the Civilian Conservation Corps, three were World War veterans and six were soldiers. The youngest was 18 years and the oldest 56 years. The average age was 25½ years.

Many of these patients received treatment for varying lengths of time at other hospitals before arriving at our institution. All such cases had been immobilized in plaster casts. X-ray taken upon admission showed poor reduction, necessitating further manipulation. For this reason, considerable time elapsed between the occurrence of the fracture and the final reduction with the Roger Anderson splint. The average time was fifteen days. The longest time was fifty-five days and the shortest was one day. The time between the occurrence of the fracture and final reduction must be kept in mind in evaluating the results in these cases.

Spinal anesthesia was given to nearly all of these patients. The pins were inserted through the upper and lower ends of the tibia. The ends of the pins were then fixed in the splint and the reduction was accomplished under di-

*Read in Section on Bone and Joint Surgery, Southern Medical Association, Twenty-Ninth Annual Meeting, St. Louis, Missouri, November 19-22, 1935.

rect fluoroscopic observation. A cast was then applied from the mid thigh to the toes.

We were not always able to obtain so satisfactory a reduction as one should expect the first time. X-ray taken the day following the reduction occasionally showed slight separation of the fragments and at times slight angulation.

I believe this was due to two factors: first inexperience with the splint, and second, a poor fluoroscopic machine, which failed to give us the necessary detail to detect these faulty conditions. These conditions were corrected by removing a small circular section from the cast at the site of the fracture, and after the corrections were made the two sections of the cast were incorporated with plaster bandages.

The average time of the double pin fixation in these cases was nine weeks. When the pins were removed the extremity was examined to see if there was union and anterior-posterior and lateral x-rays were taken. If union was not firm, as was nearly always the case, a non-padded cast was applied for a period of from four to six weeks. By this time union was usually firm enough so that support was no longer necessary. Physiotherapy was then started. When union was firm enough for weight bearing, the patient was fitted with a tibial caliper and allowed to walk. None of these patients was permitted to bear weight on the injured extremity during the period of the double pin fixation. The average time from reduction to weight bearing with tibial caliper was four and a half months.

Several patients had serious complications, such as multiple fractures, cerebral concussion, pneumonia and empyema. Such conditions can reasonably be expected to delay union by impairing vitality and slowing up the reparative powers of the body.

In seven of these cases the fractures were compound, but none developed osteomyelitis.

One case was definitely classified as non-union. This man is short and obese. He also had a trimalleolar fracture of the opposite ankle, as well as a fracture of the radius. These fractures healed in the normal time. His blood calcium and phosphorus have always been normal. Even after doing an osteotomy on the fibula and drilling the fragments of the tibia and allowing him up on a walking cast, he failed to get union. I finally did an autogenous bone graft on him about six weeks ago.

Another case, also obese, had a fracture of both legs. The right was compound and was put up in traction with a Steinman pin through the os calcis and the left leg was reduced with the Roger Anderson splint. He has been under treatment for one year. X-rays recently taken still show but little callus. The left leg now feels firm, but there is slight movement in the right. He may require a bone graft.

CONCLUSIONS

This series of cases is too small to allow us to draw very definite conclusions.

The method described has certain distinct advantages. It gives us more control of the fragments than any other method, except open reduction. Once the fracture has been reduced there is no danger of displacement. The patients do not require hospital treatment. The danger of infection is very slight and certainly less than from open reduction. Bed treatment is not necessary as in the case of traction by means of the Steinman pin or Kirschner wire through the os calcis. Compound and comminuted fractures can be treated by this method.

So far as my experience goes, the chief objection to this method is the possibility of delayed union. In our cases union certainly seemed slower than one would expect. Most of my cases were unfavorable from the standpoint of treatment by any method. The time between the original injury and the final reduction was too long to expect prompt healing. While I do not intend to use this method indiscriminately in all cases, I shall continue to use it until I am convinced that other methods are better.

DISCUSSION (*Abstract*)

Dr. W. K. West, Oklahoma City, Okla.—I have used this splint for the last several years and I have also visited Major Bolibaugh at the Walter Reed General Hospital.

In severe comminuted fractures, this appliance is ideal in that it enables the surgeon to reduce the fracture immediately and maintain the position by fixed skeletal traction, thereby enabling the patient to be ambulatory.

The fragments in serious fractures cannot be held by simply putting on a plaster cast, as we know that overriding and shortening, as well as angulation, will take place as soon as swelling recedes. Skeletal weight traction will maintain the fragments satisfactorily, but that requires long-continued hospitalization.

Dr. Austin T. Moore, Columbia, S. C.—The Roger-Anderson automatic splint is a beautifully made and very clever mechanical device. It is of decided advantage when properly used in the handling of a

great many fractures, but it can be a very dangerous machine when applied indiscriminately. There are certain mechanical and physiological points which have not been brought out in the discussion. If these points are not carefully observed a great many cases of delayed or non-union will result.

For a number of years I have been using the principle of skeletal fixation of fractures in plaster with a wire or pin above and below the site of fracture. At first I had a homemade apparatus of gas pipe frame and used bicycle spokes with a horseshoe as tautener. The wires were kept tight with lugs embedded in the plaster. There was enough slack in the wires for the bone ends to be drawn tightly together by muscle pull, and we never had delayed or non-union.

Then we bought a complete Roger-Anderson apparatus. The mechanism of the splint with its possibility of perfect control of the fragment appealed to me. But at once we began having trouble with delayed union, the explanation of which lies in the fact that rigid pins embedded in plaster hold perfect reduction, but hold it so perfectly that the ends of the bones are kept apart when absorption occurs and are not allowed to jam more and more tightly together as they would if the fracture were simply put up in a cast or other splint. It is an established fact that a certain amount of absorption takes place at the site of every fracture. Normally, muscle pull keeps the gap closed by drawing the fractured surfaces closer together as absorption occurs. If the fracture is of the transverse type and weight can be borne, this weight-bearing is very important and hastens healing by jamming the fragments together. Active use of the extremity increases the blood supply, prevents fibrosis of the soft tissue, and minimizes joint stiffness which ordinarily occurs after prolonged immobilization. I try to follow the principle of perfect and prolonged immobilization at the actual site of the fracture and active exercise with ambulation and weight-bearing wherever possible.

By injudicious use of the Roger-Anderson splint not only may the bone fragments be kept from coming together after absorption, but they may actually be drawn farther apart in the plaster cast. When one views the reduced fracture in the splint the position may appear perfect. But the ends of the pins are held in the frame and the pins are bent due to the distracting force necessary. If the cast is applied on these bent pins the fixation points are moved closer to the bone, and when the extremity is released from the splint the pins spring back into their straight position and the fragments are actually distracted to a point where they may not even be touching each other at all. With this sort of situation it is impossible for union to take place, especially after some absorption has occurred. In a number of the slides which Dr. Bolibaugh presented I noticed a definite space between the fragments and a number of the pins were bowed with the distracting force. He stated that delayed union had occurred and in one case a bone grafting operation was necessary.

To summarize, the Roger-Anderson apparatus is good when properly applied in certain selected cases. It should not be used as a routine. The inventor and all persons recommending the splint should emphasize the point that the bone ends should be jammed tightly together, even to some shortening, and that the pins should be cut out from the plaster to allow tight impaction as absorption takes place.

CHILDREN'S TEETH IN RELATION TO PEDIATRIC PRACTICE*

By J. B. Stone, M.D.
Richmond, Virginia

The care and preservation of children's teeth is a responsibility of the pediatrician as much as it is of the dentist. During the age period covered by the pediatrician maldevelopments and defects most often have their beginning, or become evident, and they are more amenable to correction than at any other time.

Incidence of Caries.—There is probably no disease so generally prevalent as dental caries. The incidence of decay among school children in the entire United States, according to the report of the White House Conference, is 95 per cent. Likewise malocclusion in varying degrees has been found to be widely prevalent.

Effects of Caries and Maldevelopment.—Dental caries may affect health in many ways. Painful conditions in the mouth not only may prevent the child from eating its normal food, but may lead to many nervous and systemic disorders. Both caries and malocclusion interfere in varying degrees with the normal process of mastication and may be responsible for serious digestive disturbances. Purulent conditions associated with carious teeth constitute foci of infection from which there may be absorption of both bacteria and bacterial toxins. Endocarditis, pyelitis, nephritis, and general septicemia have been shown in certain cases to have started from infections about the teeth. Decayed teeth along with other remediable defects have also been demonstrated to have a definite retarding influence on children's progress in school. In New York City a few years ago a study[1] was made of 67,000 children who had failed to be promoted and 80 per cent of these failures were attributed to defective teeth.

Malocclusion is not only disfiguring, but may be contributory to disorders of both the digestive and respiratory tracts.

Causes of Caries.—A close relationship exists between bones and teeth, since both are composed largely of the salts of calcium and phosphorus and their sound development depends on the proper assimilation and utilization of these materials.

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*Read in Section on Pediatrics, Southern Medical Association, Twenty-Ninth Annual Meeting, St. Louis, Missouri, November 19-22, 1935.

Heredity probably has some influence on bone and tooth formation and has been held responsible for certain anomalies of the teeth and maxillae. In certain cases dysfunction of one or more of the endocrine glands has been associated with defective dentition and abnormal bone development.

More important than the above, from a practical standpoint, is the effect on the teeth of local conditions in the mouth, faulty nutrition, and metabolic disorders.

Koehne, Bunting and Morrell[2] have correlated the presence of acid-producing organisms in the mouth with a high or increasing incidence of caries, and from their work concluded that a diet of uniform quality, containing little artificially sweetened food, and partaken of at regular times each day will control the growth of *B. acidophilus* in the mouth and the activity of caries in the majority of susceptible persons. Variation in the acid-base balance of the body fluids toward the acid side has been said to favor caries, but Boyd, Drain and Stearns,[3] after biochemical studies on a large group of children, conclude that the levels of serum and phosphorus and the acid-base relationship are not primarily of significance in the production or prevention of dental caries. On the other hand, Larsen[4] and coworkers, after studying a group of children, state that a diet in which the carbohydrates with an acid residue are replaced by alkaline starches with the addition of a small amount of vegetables results in the correction of dental defects.

Mellanby,[5] from experimental and clinical data, is of the opinion that hypoplasia is the important factor in tooth decay and thinks that a diet containing a high percentage of refined cereals contributes to that end. On the other hand, Schoenthal and Brodsky,[6] in their observations, found the incidence of caries not to be related to hypoplasia. Boyd and Drain,[7] at the University of Iowa, by their studies on the influence of diet, have emphasized its importance in the prevention and arrest of dental decay. They found that groups of children on a controlled diet of milk, cream, cod liver oil, meat, bulky vegetables and fruits, showed arrest of caries in the course of a few months. Similar results have been reported by Bunting[8] at the University of Michigan, and by Howe,[9] of Boston, and by others. Whatever difference of views may be held by different students of the problem, almost all agree that a diet nutritionally adequate is essential for the making of good teeth. All advocate practically the same type of diet: that is, one containing milk, eggs, bulky vegetables, fruits and cod liver oil, or some other source of extra vitamin D. Such a diet contains the necessary mineral elements, especially calcium and phosphorus, protein, fats, carbohydrates and vitamins that are essential for good general body nutrition.

Sound teeth are found among people in various parts of the world where there are wide differences in the food consumed. In general it has been found that better teeth prevail among those people whose diet is selected from natural foods and is consumed without undergoing processes of refinement. Wherever the native diet has been changed to one prominent in its content of refined cereal products and sugar there has been an increasing prevalence of badly formed and carious teeth.

Scope of Present Study.—The present study consists of a review of the records of several groups of children seen in private practice during the past twelve years and last examined after they were 6 years old. It was undertaken to determine whether the incidence of caries showed any relationship to: (1) the period of breast feeding; (2) the age and length of time under fairly constant pediatric supervision with regular administration of vitamin C as orange juice or tomato juice and of vitamin D in the form of cod liver oil, viosterol, halibut liver oil, ultraviolet light, or combinations of these; (3) the socio-economic status; and (4) the general nutritional condition.

The observations were all made by the author in the course of routine physical examinations. Occurrence of caries has probably been understated in all of these groups, as a careful examination made by a dentist would no doubt have revealed a much higher incidence of decay. However, the same error would run through all the groups, and for comparative purposes would not be of great importance.

Effect of Breast Feeding.—A group of 66 children with a history of breast feeding for not more than one month was compared to a group of 139 said to have been breast fed for six to twelve months (Table 1). In both of these groups the first examination was made at 4 years or past and the final examination after the child was 6 years old. In the group having little or no breast feeding 53 per cent were recorded as showing no caries, whereas in the group breast fed for six to twelve months only

Table 1

DENTAL CARIES AND BREAST FEEDING

	Breast fed 1 month or less, first examined at 4 years or older and last examined at 6 to 12 years.		Breast fed 6 to 12 months, first examined at 4 years or older and last examined at 6 to 14 years.	
	No. Cases	Per Ct.	No. Cases	Per Ct.
Without caries	35	53	63	45.3
1 or 2 carious teeth	6	9	16	11.5
Several carious teeth	21	31.8	48	34.5
Many carious teeth	4	6	12	8.6
Total number recorded	66		139	
Average age at last observation	7.8 years		8.2 years	

45.3 per cent. Further analysis of the two groups, when subdivided according to whether one or two teeth, several, or many were carious, fails to show any advantage of the breast fed over the non-breast fed. The range of ages and the average age at which the final examination was made were very nearly the same in the two groups, though slightly greater for those who were longer breast fed. This might account to some extent for the slightly greater incidence of caries shown in the latter.

Children First Seen Before the Age of Six Months Compared with Those First Seen Between Six and Twelve Months.—A comparative analysis was made of 130 children under observation beginning at six months or earlier and 23 children under observation beginning at six to twelve months, both groups remaining under observation until after 6 years of age. The incidence of caries was noted after 4 years of age (Table 2). These groups are subdivided according to their socio-economic status into good, fair and poor. Vitamin D in the form of cod liver oil, viosterol, halibut liver oil, ultraviolet light or combinations of these, as well as vitamin C in the form of orange juice or tomato juice had been prescribed for both groups throughout infancy and early childhood. In the feeding instructions for both groups, when old enough for mixed diet, stress had been laid on the importance of milk, coarse vegetables, fruits and eggs or lean meat as the essential part of the daily diet. In spite of the prescribed diet there is found a rather high incidence of caries in both groups. In each of these two groups, those of good socio-economic status show a slight advantage over those whose status is classified as fair or poor, with the exception of one sub-group where the number of cases was too small to be significant.

In the group first observed prior to six months the percentage without caries in the good, fair and poor classifications, respectively, was 54.8, 45.8 and 7.7. In those first observed between six and twelve months there is found the same relatively lower incidence of caries in the good socio-economic group when compared to the fair group. The number of cases in the poor group is too small to be considered. The percentage without caries in the good and fair classes, respectively, was 71.4 and 28.6. Combining the last two groups (shown in Table 2) to make a larger group of 153 cases consisting of those under observation from twelve months

Table 2

CARIES AND ECONOMIC STATUS

Socio-economic Group	130 children under observation from 6 months or earlier to 6 years or later. Incidence of caries noted after four years of age.						23 children under observation from between 6 and 12 months to 6 years or later. Incidence of caries noted after 4 years of age.					
	Good		Fair		Poor		Good		Fair		Poor	
	No. Cases	Per Cent	No. Cases	Per Cent	No. Cases	Per Cent	No. Cases	Per Cent	No. Cases	Per Cent	No. Cases	Per Cent
Without caries	51	54.8	11	45.8	1	7.7	10	71.4	2	28.6	2	100
1 or 2 carious teeth	10	10.7	2	8.3	1	7.7	2	14.3	2	28.6	0	0
Several carious teeth	22	23.6	7	29.1	7	53.8	2	14.3	2	28.6	0	0
Many carious teeth	10	10.7	4	16.6	4	30.8	0	0	1	14.2	0	0
Total number of cases	93		24		13		14		7		2	
Average age of last examination	7.3 yrs		6.9 yrs		7 yrs		8.1 yrs		7.1 yrs		6 yrs	
Age range at last examination	6-10 yrs		6-9 yrs		6-10 yrs		6-12 yrs		6-9 yrs		6 yrs	
Percentage combined groups without caries	48.5						60.8					

or earlier until after 6 years of age there is shown more strikingly the advantage of those in the better socio-economic class (Table 3).

Table 3

CARIES AND ECONOMIC STATUS

153 children under observation from 12 months or earlier to 6 years or later. Observations made after 4 years of age (two previously analyzed groups in Table 2 combined).

Socio-Economic Group	Good		Fair		Poor	
	No. Cases	Per Cent	No. Cases	Per Cent	No. Cases	Per Cent
Without caries	61	57	13	41.9	3	20
1 or 2 carious teeth	12	11.2	4	12.9	1	6.6
Several carious teeth	24	22.4	9	29	7	46.6
Many carious teeth	10	9.3	5	16.1	4	26.6
Total	107		31		15	
Average age at last examination	7.7 yrs		7 yrs		6.5 yrs	
Age range at last examination	6-12 yrs		6-9 yrs		6-10 yrs	

In the good socio-economic group 57 per cent failed to show tooth decay; in the fair group only 41.9 per cent, and in the poor group only 20 per cent. In the subdivisions of those showing one or two, several or many carious teeth this same advantage holds. It is especially evident in the case of those noted as having several carious teeth, the percentage of these in the good group being 22.4, in the fair group 29, and in the poor group 46.6.

Children First Examined After the Age of 4 Years. — Three hundred forty-eight children (Table 4) first seen after they were 4 years old and under observation until after 6 years were analyzed as to the relationship of caries to the socio-economic status. Here again the incidence varied directly with the socio-economic condition. In the good group, 57.8 per cent failed to show tooth decay, whereas in the fair group the percentage had dropped to 42, and in the poor group to 27.4. In the subdivisions based on the amount of caries, the greater number fall in the group having several carious teeth and the percentage here increases in going from the good to the poor group, in spite of the fact that the age at the time of the last examination

Table 4

DENTAL CARIES AND EARLY PEDIATRIC CARE

348 children first examined after 4 years old and under observation at 6 years or later.

Socio-Economic Group	Good		Fair		Poor	
	No. Cases	Per Cent	No. Cases	Per Cent	No. Cases	Per Cent
Without caries	99	57.8	53	42	14	27.4
1 or 2 carious teeth	20	11.6	10	7.9	5	9.8
Several carious teeth	44	25.7	53	42	22	43.1
Many carious teeth	8	4.6	10	7.9	10	19.6
Total	171		126		51	
Average age at last examination	9 yrs		7 yrs		7.8 yrs	
Age limits	6-15 yrs		6-14 yrs		6-14 yrs	

Table 5

DENTAL CARIES AND EARLY PEDIATRIC CARE

	Under observation from 12 months or earlier to 6 years or later. Observations made after 4 years old.						First examined after 4 years old and under observation at 6 years or later. Observations made after 4 years old.					
Socio-economic Group	Good		Fair		Poor		Good		Fair		Poor	
	No. Cases	Per Cent	No. Cases	Per Cent	No. Cases	Per Cent	No. Cases	Per Cent	No. Cases	Per Cent	No. Cases	Per Cent
Without caries	61	57	13	41.9	3	20	99	57.8	53	42	14	27.4
1 or 2 carious teeth	12	11.2	4	12.9	1	6.6	20	11.6	10	7.9	5	9.8
Several carious teeth	24	22.4	9	29	7	46.6	44	25.7	53	42	22	43.1
Many carious teeth	10	9.3	5	16.1	4	26.6	8	4.6	10	7.9	10	19.6
Total number of cases	107		31		15		171		126		51	
Average age at last examination	7.7 yrs		7 yrs		6.5 yrs		9 yrs		7 yrs		7.8 yrs	
Range of ages at last examination	6-12 yrs		6-9 yrs		6-10 yrs		6-15 yrs		6-14 yrs		6-14 yrs	

is slightly greater in the good socio-economic division than in the others.

Comparison of Those First Seen Before the Age of 12 Months with Those First Seen After 4 Years.—Comparing the 153 children (Table 3) under care since early infancy with the 348 children (Table 4) first examined after the age of 4 years, there is found (Table 5) very little difference in the amount of caries among those of corresponding socio-economic status in the two groups. The greater number of those showing caries fall in the subdivision having several decayed teeth, and in this subdivision a moderate advantage is shown in the good and fair socio-economic classifications for those who had been under observation since early infancy, with close supervision of their diet and general health.

Incidence of Caries Relative to Nutritional Condition.—The nutritional condition of 377 children (Table 6) noted at the time of their first examination when they were four years of age or older was classified as good, fair or poor and the incidence of caries in these groups was compared. The nutritional classification was not based solely on a fixed standard of weight, but on the physical examination with reference to the general appearance of physical fitness, color, muscle development, tone of skin, and posture, considered in conjunction with the weight and height.

It was observed that the percentage of those children showing no caries was very nearly the same in the groups whose nutrition had been recorded as good or fair, but distinctly lower in the poor group. The subdivisions indicating the amount of caries present also showed that where the decayed teeth had been recorded as many the percentage of caries was much higher in those whose general nutrition was poor.

Table 6

CARIES AND NUTRITIVE STATE

Incidence of caries relative to nutritional condition noted at time of first examination in children 4 years of age or older.

Nutrition	Good		Fair		Poor	
	No. Cases	Per Cent	No. Cases	Per Cent	No. Cases	Per Cent
Without caries	67	54	100	53.7	31	46.2
1 or 2 carious teeth	15	12	16	8.6	5	7.4
Several carious teeth	36	29	57	30.6	22	32.8
Many carious teeth	6	4.8	13	6.9	9	13.4
Total number of cases	124		186		67	

COMMENT

The data here presented differ from what was expected when the study was undertaken. Children with a history of breast feeding for six to twelve months showed no better deciduous teeth than those breast fed less than one month. The group that had been under observation from early infancy and for whom the diet prescribed was in keeping with what has been accepted as balanced and adequate showed about as high an incidence of caries as those first coming under observation at a later age, whose diet may or may not have been in accord with recognized standards.

The above findings bring to mind several questions. The first is the effect of prenatal influences on the structure of the deciduous teeth and their later susceptibility to decay. Since a considerable degree of calcification of the deciduous teeth takes place before birth, it seems reasonable to assume that the mother's diet and health would have a definite effect on their structure and their later resistance to decay.

The second question is that of the effectiveness with which prescribed diets are carried out in the home over a long period of time. There is often a wide gap between the knowledge of nutritional needs and the practical application of that knowledge. Over a period covering a number of years adherence to a diet that contains the essential foods is less apt to be continued than is true of shorter periods of observation. In the home environment the child's taste and desire for certain foods often take precedence over the physician's instructions in controlling the dietary. Although the incidence of decay was about the same in the children under supervision from early infancy as in the other groups, it was noted that, in the former, caries was less destructive, and the teeth were better preserved by more prompt dental restoration, when decay had made its appearance.

The failure of the supervised children to make a better showing in the tables presented might also be partly explained by the fact that those in the other group in many instances had been seen only once or a few times and in the pediatric examination small cavities were probably overlooked, whereas similar conditions would have been detected and recorded for those

who were examined regularly several times a year.

In all the groups studied better teeth were found in those children in the better socio-economic class. This might be attributed to better oral hygiene and more regular visits to the physician and dentist as much as to any difference in the diet itself.

Finally it was observed that, as a whole, children with good general body nutrition showed less caries than those whose nutrition was recorded as fair or poor. This is in accord with the view that the health of the teeth is to a considerable degree a matter of nutrition; that they give early indication of a nutritional deficiency, and may be affected by deficiencies that are too small to show up grossly in other organs.

Since calcification of the first permanent teeth does not begin until just before or shortly after birth, and the process of calcification of all the permanent teeth goes on actively throughout childhood, it seems reasonable to suppose that the child's diet would have a more pronounced influence on these than on the deciduous teeth.

The importance of taking care of the primary teeth is greatly underestimated by many people. As pointed out by Sweet[10] and associates, it is the duty of the pediatrician to impress on them the importance of the function of these teeth. Not only because of their relation to the permanent teeth and the part that they play in maintaining the shape of the alveolar processes, but because they are needed for purposes of mastication until replaced by the permanent teeth, they should not be neglected. Unless the time for their normal loss is near at hand they should not be removed if their restoration is possible. If they have become so diseased that restoration is not possible, they had best be removed on account of the danger of resident infection within the mouth.

SUMMARY AND CONCLUSIONS

(1) It has been demonstrated experimentally and clinically by other investigators that dental hypoplasia and caries can be definitely influenced by diet, and that the consumption of a diet containing liberal amounts of dairy products, eggs, bulky vegetables, fruits and cod liver oil is effective in the prevention and arrest of both hypoplasia and caries.

(2) The present report is based on a study of a small group of cases observed under conditions prevailing in private practice and the findings are to be regarded as suggestive rather than conclusive.

Children with a history of breast feeding for six to twelve months showed as high incidence of caries as did those breast fed only one month or less.

Children under supervision from early infancy whose prescribed diet included the so-called essential foods and cod liver oil or its equivalent showed about as high incidence of caries as those first observed after 4 years of age and whose feeding histories suggested a less adequate type of diet. However, in the former group it was noted that the caries was usually less extensive and restorative work was done before advanced destruction of the teeth occurred.

It was found that in those children of good socio-economic status, with good general body nutrition, both the incidence and the extent of caries was less than in those of poor socio-economic status or with poor nutrition. This would seem to indicate that the formation and preservation of sound teeth is closely related to good care and to good general health.

(3) There is need for more effective application of known facts regarding the relationship of diet, nutrition and tooth decay. Even when all available knowledge of this subject is utilized it seems that caries inevitably occurs in the deciduous teeth of a large number of children. Since it is the physician who has the first contact with the child, he has the earliest opportunity for advising those measures that have been shown to favor sound teeth. After maldevelopment or caries have made their appearance it is ususually he rather than the dentist who first has the opportunity for detecting the defects in the incipient stage. He should be constantly on the lookout for such conditions and, when they are found, explain to the parents the importance of prompt corrective work. With the cooperation of a competent dentist, and by inclusion in the diet of those things known to have a favorable influence on the arrest of caries, and by other measures that will make for the child's best general health, much can be done to prevent further progress of the destructive process.

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DISCUSSION (*Abstract*)

Dr. Edward Clay Mitchell, Memphis, Tenn.—This subject may be discussed under the following subheads, which are given in order of their importance: (1) heredity and family predisposition; (2) prenatal influences; (3) diet and dental care; (4) habit; and (5) focal infection.

(1) I believe sufficient emphasis has probably not been attributed to heredity. We all know that the contour of the face is often determined by family transmission, even without other cause. We know, further, if we have kept careful records of our cases that certain families regardless of diet, environment, or habit, have good teeth with few caries. Just what this influence is we are not able to determine. In a recent survey of children's teeth in Memphis City schools, a prize was offered for the child in grammar school having the best set of teeth and the cleanest mouth. The prize was won by a 12-year-old girl from a comparatively poor family. She had twenty-eight teeth, free from caries and with scarcely any discoloration, even though she had never owned a toothbrush. Further investigation showed that the older sister of this child had previously won a similar contest. A grandfather, 72 years old, in the same family had remarkable teeth, even though he had been a tobacco chewer all his life.

(2) It is a well-known fact that the deciduous teeth begin to calcify at about the one hundred fortieth day of life, are fully formed at full term, and the permanent teeth have begun to calcify. Both disease of the mother and her diet and general care have a definite influence on this calcification. The old saying "A tooth for every pregnancy" in the mother was true. If she were deprived of proper diet she gave her calcium to her infant, but this was insufficient.

(3) The civilized diet, especially the fully prepared food that requires no mastication and is high in carbohydrates, is undoubtedly detrimental to proper formation of teeth. The skulls of the American Indians in the Smithsonian Institution with few exceptions show uniformly good teeth. The Eskimo in his native heath has good teeth, but remove him to a different environment and his teeth become bad. I made the statement a few years ago that the teeth of the East Indians, where large quantities of milk were about the only diet, were exceptionally good, though the toothbrush was virtually unknown. I was called to account by Dr. Sweet, of California, who brought out the fact that these natives polish their teeth by chewing betel root sometimes for hours a day.

Dr. May Mellanby, writing on the use of cod liver oil and vitamin D, indicates that in the British Isles marked decrease of dental caries resulted from the consumption of these vitamins. The experimental work done by Howe on rats with vitamin C is interesting. The work of Boyd and Drain showed that children who were fed diabetic and celiac diets were less affected by dental disease. Their subsequent work on milk was of value, in which they demonstrated that a quart of milk daily furnished calcium very necessary for proper tooth formation. Breese, of London, observed that 600 children in a British orphanage had a lower percentage of dental caries than children found in his private practice in better families. The diet of the children in the orphanage was low in sugar. Fruits were substituted for desserts. He also says that in England during the War, when sweets were limited, caries was decreased in children. He strongly objects to the theory that diet controls caries by strengthening the teeth, and says that no enamel is strong enough to resist the acids of caries. He draws a comparison with the use of hair tonics for the prevention of baldness. So it would seem that a plain, substantial diet, with plenty of vitamins, particularly A, C and D, sufficient roughage to induce mastication, and low carbohydrates to lower the acids in the mouth is proper, and that the best results would be obtained by this diet.

(4) Thumb sucking, pacifiers and other habits of this kind tend to produce malocclusion as well as bad breathing from adenoids. Malocclusion prevents proper mastication; as a result the gums become sore and the teeth are also affected.

(5) There is another phase of the teeth in children that deserves mention: that is, focal infection, even sometimes in the young child. Baby H., aged 4 years, developed a typical case of rheumatic fever. The tonsils and adenoids were removed. There was little improvement. The case continued for 1½ years, although the gums appeared healthy and the deciduous teeth appeared to be in good condition for a child that age. X-ray of the teeth showed an abscess between one of the permanent molars not erupted and the baby tooth. This baby tooth was extracted, the pus drained off, and the child made a prompt recovery. This is only one of several cases that I have seen of like nature.

In closing, I should like to say that the best results are obtained by proper consideration of all of the above factors. In my experience the best teeth are not found in the highest walks of life. I should like to emphasize again that heredity is the most important factor; that plain substantial diet, moderate in carbohydrates and containing sufficient vitamins, and also enough roughage to require mastication, is probably best. Early dental care is certainly important, as good teeth are essential for proper child health.

Dr. William Weston, Jr., Columbia, S. C.—I like to classify the teeth and gums as the first line of defense in evading disease and in the protection of health. When the normal construction of the elements (enamel, pulp, and so forth) of the tooth is interfered with, we invite carious teeth, which in turn furnish a fertile field for infection. It is similar to a faulty steel pillar in a building, for no chain is stronger than its

weakest link. There is, as Dr. Stone has pointed out, sluggishness in the school work of those who have deciduous teeth and malocclusion. How can this be prevented?

I should like to emphasize the importance of dietary measures which of necessity must commence early. By this I mean early in pregnancy. It is in this stage of development that the correct or incorrect alveolar processes are formed which have a tremendous bearing on both the teeth and jaw. The chemical elements of food, both the mineral elements and the vitamins, are interdependent in their utilization by the body. Though calcium and phosphorus are the elements which make up a large part of the teeth, magnesium must be present and all of these must be properly balanced by iodine and a small quantity of iron. It is equally true of the vitamins. We are assured that A, D and C, especially the latter, are concerned.

Mellanby has proven experimentally that deciduous teeth can be produced under decalcifying influences, then decalcification may be checked by adding the essential constituents. Provitamin A or carotene is necessary in the prevention of infections. Higgins and his associates have demonstrated the disappearance of ureteral and kidney stones at the proper hydrogen ion concentration of the body with the addition of provitamine A, which stimulates epithelial growth.

You have heard of persons who have a full stomach yet are starving, which means that food bulk is available, but the nutritional value is not present in the correct proportions. When the cuticle and germ portions of the cereal grains are removed, as is done in refining processes, the nutritional value of these foods which are universally prescribed for infants and children is greatly impaired. The heart of the cereal remains, but the very life is absent.

It is not the kind of tooth paste or toothbrush one uses, nor is it the frequency of application, but it is essentially the kinds of foods which are chewed and digested that determine the character of the teeth. Milk, regardless of whether it is mother's or cow's, is essential to the formation of the skeletal system, particularly the teeth. I will go further to add that the quality of the milk of the lactating animal depends largely upon the food it eats.

In conclusion, may I call to your attention the fact that teeth are one of the very best indices as to the dietary sufficiency or deficiency. Therefore, a discussion of this subject is always beneficial and timely.

Dr. J. R. Lemmon, Amarillo, Tex.—I wish to call attention to a distressing and serious dental staining known as mottled enamel and "brown stain" of teeth which occurs endemically in the Texas Panhandle-Plains area, the largest known endemic area in the United States. I called attention to this condition in a paper, "Mottled Enamel of Teeth in Children," in the *Texas State Journal of Medicine* in September, 1934.

Mottled enamel, a tooth defect, first reported by Black and McKay in 1916, is endemic in certain communities in Texas, Arizona, Colorado, New Mexico, Oklahoma, Kansas, Virginia, Arkansas, Illinois, North and South Dakota, Holland, China, Spain, South America, South Africa, the Bahamas, and Cape Verde Islands. The condition is by no means so rare as was formerly thought and bids fair to become a serious menace to young tooth structure in many areas.

The child's teeth present dull, chalky white or paper white patches irregularly over the teeth, chiefly the upper central incisors. The teeth glair unnaturally and produce a serious cosmetic defect. Many cases are stained rust color and resemble spots of adherent rust or flakes of chewing tobacco. The enamel is often pitted and eroded, and tends to decay easily. The staining is in the permanent teeth almost entirely and cannot be removed without damage to the enamel.

Mottling of the teeth is definitely due to the fluorine content of the drinking water, which usually comes from deep wells, although in Colorado it may be caused by the so-called pure mountain water. In the Amarillo, Texas area our water supply comes entirely from windmill wells or fairly deep city water well supply and the fluorine content is usually about 4.5 parts per million. A large percentage of native children are doomed to have teeth with mottled enamel.

The problem involves cosmetic effects on the patient; it involves the pediatrician, the dentist, the public health service, the food and water supply in endemic areas, and may cause a complete change in the water supply of whole municipalities and regions affected.

Prophylaxis lies in the proper pre- and post-natal diet, the use of calcium, plus elimination of the drinking water (and possibly food) with moderate fluorine content in the endemic areas.

MALARIA IN CHILDREN*

By W. Pierre Robert, M.D., F.A.A.P.
Vicksburg, Mississippi

The following remarks on malaria in children are offered as further illustration of the fact that the pediatrician is more than a general practitioner limiting his practice to patients under thirteen years. There is a vast difference in this disease in children and in adults, more than is found in rheumatism or typhoid fever or pneumonia.

That malaria is at present a very real problem is borne out by extracts from a recent paper by Henry Hansen,[1] Chairman of the National Malaria Committee. This author says that the eradication of malaria is not appreciably closer at hand than it was in 1916. He, in company with the other members of this Committee, does not feel particularly optimistic of accomplishing its eradication. Their hope now is to accomplish a fair degree of control. Because of the difficulty in obtaining accurate information from practicing physicians the morbidity and mortality reports on malaria are far from accurate, yet all of the available data point to a marked

*Read in Section on Pediatrics, Southern Medical Association, Twenty-Ninth Annual Meeting, St. Louis, Missouri, November 19-22, 1935.

*From the Vicksburg Clinic, Vicksburg, Mississippi.

increase in both for the years 1933 and 1934. The mortality statistics for the fourteen Southern states for the year 1933, according to Faust and Diboll,[2] show a marked increase in every state except North Carolina. Not only has there been a marked increase in the number of cases of malaria, but the parasite has extended into states hitherto comparatively free. In my home city of Vicksburg, in Warren County, Mississippi, malaria is hyperendemic. By this, I mean it is present during the entire year. To give you some idea of the incidence of malarial infection among the school population in Mississippi, I am inserting the following figures given to me by Dr. Geo. E. Riley, of Jackson, Mississippi, Director of Malaria Control:

This survey of March and April, 1933, was made in 110 white schools and 64 colored schools, or a total of 174 schools. Slides were taken on 13,296 white children, 5,858 colored children, or a total of 19,144. The samples of all age groups other than those from 5 to 19 years were so small as not to be significant. The results in the three age groups, 5-9, 10-14 and 15-19, were as follows:

Age Group	White			Colored			Total		
	No. Taken	No. Pos.	Per Cent Pos.	No. Taken	No. Pos.	Per Cent Pos.	No. Taken	No. Pos.	Per Cent Pos.
5-9	6,493	269	4.1	2,158	151	7.0	8,651	420	4.9
10-14	5,491	325	5.9	2,657	267	10.0	8,148	592	7.3
15-19	1,023	40	3.9	712	72	10.1	1,735	112	6.5

Note that the incidence of positive smears in negroes approximately doubles that found in whites. The incidence is comparatively low in the 5-9 age group and were figures available would be even lower in those under 5 years, as these children are better protected from the Anopheles mosquito during its feasting hours, namely, from sundown to sunup. Malaria, widely distributed throughout tropical and subtropical countries, has been encountered at the extreme latitudes of 40 degrees south and 60 degrees north. To stamp out malaria we must either destroy the parasite, destroy the mosquito or destroy the patient. Only the first alternative will be considered in this paper.

It seems now to be definitely proven and generally accepted that we have such a thing as congenital malaria. Most contributors to the literature on this subject stress the filtering quality of the syncytium as being the important factor in the prevention of malarial infection of the newborn. Some writers believe that the newborn is never infected unless there has been a placental injury, but Mackay[3] (malaria research officer, Dar es Salaam), suggests that placental ferments are responsible for this protection. In twenty-two of this author's cases smears were taken from the maternal side of the umbilical cord, the fetal side of the cord and from the child's heel. In no instance was the plasmodium found in the blood from the fetal end of the cord, but it was found three times from the maternal side and seven times from the child's heel. He concludes that in an apparent infection rate of 33 per cent not one parasite was demonstrable as coming from the fetal side of the severed umbilical cord, although in smears from the maternal side the malarial parasites did overcome the resistance of the syncytium and appear in the fetal circulation. Regardless of the mechanism, it is a fact that congenital malaria would be found more often if looked for. It would be interesting to know what part it plays in infant mortality.

At this point I wish to bring out and emphasize the fact that in hyperendemic areas malarial infection is maintained principally by the child population. It has been known for some time that adults develop an immunity or acquired resistance to this infection. James (1931) reported the results of a study where 1,365 individuals were fed upon by mosquitoes infected with *Plasmodium vivax* and only 72.5 per cent developed the infection. Cuica[4] *et al.* reported 53.3 per cent developing the infection after being infected with *Plasmodium vivax*, 61.3 per cent with *Plasmodium malariae* and 80 per cent *Plasmodium falciparum*. Of those infected, 18.6 per cent of the tertian, 15 per cent of the quartan and 18 per cent of malignant tertian had parasites in the blood without showing symptoms and recovered without medication. In addition these authors found that repeated inoculations with blood infected with *Plasmodium vivax* conferred immunity. This was not true of *Plasmodium falciparum*. James stated that this acquired immunity in his cases was strain and not species specific. Numerous observers have agreed that in hyperendemic areas the incidence and intensity of infection decreases with increasing age, but Kliger and Mer,[5] working for the Hebrew University in Jerusalem, reviewed the previous literature and published their findings in a paper entitled "The Development of Immunity Against Malaria in Children Under Ten Years of Age." They state that in hyperendemic areas the infection is maintained principally by the child population. Authorities

agree that children acquire an immunity very slowly. Young children are slow to form antibodies, not only to malaria, but to nearly all bacterial and virus infections. Kliger and Mer conclude that children under 6 years of age are less capable of developing a resistance or immunity to malarial parasites than are those above that age. Those under 6 years respond less rapidly to treatment and have a higher relapse and reinfection rate. The intensity begins to decrease after four years of age, but the incidence only after 6. From the above statements it is evident that to eradicate malaria by destroying the plasmodium our attention must turn to the child population. Since children have little or no resistance to the infection, some drug must be found to rid all cases and carriers of the sexual form of the parasite. Plasmochin will serve the purpose, but its administration is not without danger and the proper dosage for infants has not yet been determined. Quinine is safe, but is an effective sterilizer in only a small percentage of cases. As stated by Kliger and Mer, the therapeutic efficacy of a drug should be checked by its effect on children below six years of age because here we have not the acquired resistance to help.

In addition to this lack of resistance in children, there are some well established differences in the type of manifestation after infection has taken place. Often children who have contracted malaria will have convulsions instead of chills. Others will show blueness of the hands, feet and finger nails. As brought out by Mulherin,[6] of the University of Georgia, in 1922, there are a goodly number of babies who have malaria yet do not run fever or give a history of having had any. Some of these are breast-fed and simply lose interest in nursing, become anemic and lose weight. Unless malaria is suspected, these infants would have the breast taken from them and various foods, probably inferior, substituted, all to no avail. Their response to the proper treatment is remarkable. The fever, when present, is rarely regularly intermittent. More often it is absent, remittent or irregularly intermittent. This is no doubt due to the peculiarity of the child as host, the parasites not following the old rule, but maturing more continuously. In children the symptoms are most often referable to the digestive tract. Vomiting is present in approximately 80 per cent of the cases. Abdominal pain is a common and often misleading symptom. Diarrhea occurred in 25 per cent of Mulherin's cases. Latent tetany or a tendency to asthma and bronchitis are easily excited into activity by malaria. Headache is present in about 99 per cent of cases. Even though the infant cannot talk, he tells you plainly that his head hurts. The spleen is always enlarged in cases of long standing, but this enlargement occurs later than it does in the adult. As in adults, the largest spleens are seen in tertian malaria.

It is important to remember when examining the blood that often we are unable to find the plasmodium, due to the fact that small doses of quinine or some chill tonic containing this drug have been administered to the patient before he seeks our advice. Personally, I do not delay treatment until a positive smear is obtained, but do get several smears, if possible, because the type of malaria found will influence the drug dosage to be used and its method of administration. Although a leukopenia is generally present, this is not invariably the case. Mitchell,[7] Professor of Pediatrics at the University of Tennessee, reports a number of cases of malaria with white cell counts of 22,500 and with an increase in polymorphonuclear neutrophils. He states that the chest is clear in these cases, but that all have a slight though not severe tonsillitis. Quite often in my own practice I have noted a high leukocyte count with more than 80 per cent polymorphonuclear neutrophils in cases of uncomplicated malaria. At least if complications were present I was unable to discover them. These children had estivo-autumnal malaria. It is wise to bear in mind the fact that, although a leukopenia is the rule, a leukocytosis does not rule out malaria, even though there is no coexisting infection. No remarks concerning the diagnosis of malaria would be complete without mention of the serological tests (ferro-flocculation and melano-flocculation) devised by Henry several years ago. There have been modifications of his original work and the reports appear promising. The tests will probably be of value in detecting latent cases of malaria and in indicating when the infection has entirely disappeared. Those interested in this subject will find an excellent review of it published in the SOUTHERN MEDICAL JOURNAL of last August by Wendell Gingrich,[8] of Galveston, Texas. The diagnosis of malaria in the infant and young child is at times quite difficult and all extraneous aids should be used. One worth remembering is the observation of Bouyoucas that parasites, though absent from the peripheral blood at the initial examination, may be found following the administration of epi-

nephrin. Following this maneuver, they persist for two or three hours and then disappear.

The limitations of time and space will permit only a few remarks concerning the treatment of malaria. Mitchell,[9] before this Association one year ago, reviewed his experience with atabrine and plasmochin. Infants whom I have treated have with difficulty, if at all, retained atabrine, and because of the danger inherent in the use of plasmochin in the very young, due probably to the lack of standardization of dosage, my personal preference is almost exclusively for quinine. Because of the infant's lack of resistance to the infection, however, the dose necessary to prevent or cure is much larger than we have been taught. Unless vomiting exists or the patient is comatose or there is some good reason for extreme haste, quinine should be given by mouth. The intramuscular route is safe and is effective. Physicians are too prone to use "shots" for everything and the layman in Vicksburg has reached the place where he almost demands that his malaria be treated with "shots." Few believe, if told, that all they are getting in the vein is quinine or at times neoarsphenamine. It is seldom necessary to be radical with infants and children who have malaria, and with very few exceptions the less intravenous therapy is employed the better. While the drug treatment is all important, we must view the organism as a whole, and it is essential that the general nutrition of the patient be kept at a high level. The digestive tract of the infant and young child is easily upset during health and much more easily so during sickness.

Before completing my remarks I wish to bring to your attention a condition that is often associated with malaria. Whether or not it represents a true complication I am not prepared to say. I refer to pyelitis which occurs in a malarial patient. About eight years ago, while making ward rounds at the Tennessee Coal, Iron and Railroad Company Hospital in Fairfield, Alabama, I saw a 6-months-old female who had been in the Hospital for two weeks because of a severe pyelitis. The urine was still loaded with pus, the white blood count was 30,000 and the temperature septic in type. A blood smear at this time was positive for tertian malaria and after seventy-two hours of quinine therapy the patient had a normal temperature and the urine was entirely clear. I have treated many similar cases since that time and for these I employ the term, malarial pyelitis. Those of you who may encounter refractory cases of pyelitis in infants and young children should be careful to rule out malaria and if this cannot be done, to administer quinine in curative doses.

In conclusion I wish to report fifty cases of malaria from my own practice. All of the patients were ill enough to be hospitalized. Thirty were infected with estivo-autumnal and twenty with tertian malaria. Fifteen of the estivo-autumnal cases were admitted in coma, with one death. Twelve of the patients with estivo-autumnal malaria had white blood counts of 20,000 or higher and showed 70 to 90 per cent polymorphonuclear neutrophils. Four patients with estivo-autumnal infection and four with tertian infection had malarial pyelitis. Three patients in the tertian group had blackwater fever. Three of the patients were under one month of age and one was only one week of age and weighed but two and one-half pounds. I have not personally had a proven case of congenital malaria, but three newborns under my care did not gain in weight until given quinine. These babies were premature, the early labor in each instance had been provoked by malaria in the mother. In reviewing the records for the remaining patients suffering with malaria that have come under my care, I find that of the cases so diagnosed, the laboratory offered confirmation in only 38 per cent.

SUMMARY

(1) The problem of malaria control is far from solved. During the past few years the morbidity and mortality have increased.

(2) That we have congenital malaria is a proven fact. The condition should be kept in mind and searched for more often.

(3) In hyperendemic areas malarial infection is maintained principally by the child population. This is explained by the fact that young children develop an immunity very solwly.

(4) At present there is no safe and effective sterilizer, but plasmochin will prove valuable if the dose can be standardized for infants.

(5) Other differences between childhood and adult malaria are: (1) the frequent absence of fever; (2) its irregularity, if present; (3) the predominance of digestive symptoms; (4) the common excitation into activity of latent conditions; (5) the relatively large doses of quinine necessary to cure.

(6) While a leukopenia is the rule, many cases of malaria (estivo-autumnal in my practice) have a high leukocyte count with a high percentage of polymorphonuclear neutrophils.

(7) Quinine in large doses is the safest drug to use in children. It is seldom necessary to use the intravenous route.

(8) In treating malaria as in treating all other conditions the general condition of the patient must be kept in mind.

(9) Attention is called to a pyelitis that often exists in a malarial patient, possibly overshadowing the primary condition, but clearing quickly under proper therapy.

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DISCUSSION (*Abstract*)

Dr. N. C. Womack, Jackson, Miss.—Malaria is still a serious problem in the South. In spite of increased knowledge of its spread, better training among medical men, a broader knowledge of its control by the laity, it is on the increase.

Practically 6 per cent of the school children, white and colored, included in Dr. Robert's statistics are infected with malaria, and consequently are a source of danger to others.

In a recent examination of 107 boys just out of school, preparing to enter Boy Scout camp, 9.2 per cent were found infected with malaria parasites.

Kendall states that among a large group of children selected at random under 15 years of age, living in tropical climates, 56 per cent were positive microscopically, and in a larger group of adults 32.2 per cent were positive.

The control of malaria is a job for the engineer, the health official, the physician and the educator. Every phase of the subject from the destruction of the breeding ground to a thorough knowledge of its control by the laity, and the elimination of the carrier, will be necessary to control the disease.

Dr. Edward Clay Mitchell, Memphis, Tenn.—I wish to emphasize Dr. Robert's statement that although a great deal of money and effort have been spent on malarial control, this disease appears to be quite as prevalent in many localities as formerly. More care should be devoted to diagnosis. Every state in the South and every large city now provides laboratory facilities for diagnosis. Mosquito control has been thoroughly studied and well conducted campaigns have resulted from this study, but possibly enough time and energy have not been devoted to the eradication of the malaria carrier.

There is a section of Dr. Robert's paper with which I must take exception, and that regards the treatment. In a recent article read before the Texas Pediatric Society I reported 300 cases of proven malaria treated with atabrine and plasmochin in the Memphis General Hospital, which is under the supervision of the University of Tennessee. At the same time I stated that Dr. McElroy had treated approximately 1,200 cases in the adult at the same institution. Our results would show: first, that in the tertian type of malaria atabrine given 1½ grains daily in the adult for a five-day period, the dosage in children corresponding for the age and size, but relatively large, was sufficient to destroy both the sexual and asexual forms of parasites; that in the estivo-autumnal form the atabrine was sufficient to destroy the asexual form given in the same size dose and over the same period; for the sexual form we give routinely 1/3 of a grain daily as the maximum adult dose of plasmochin for five days for this entire series of cases.

Our findings were that atabrine was as effective as quinine in destroying the asexual type of parasite. It did not act quite so quickly in preventing symptoms as quinine. In some instances we had to give atabrine two or three or four days before the chills and rise in temperature ceased.

After giving the course of atabrine and plasmochin the blood was examined and the case was not discharged until the blood was parasite free. The symptoms universally disappeared after five days' medication, though the blood, in many instances, showed parasites which eventually disappeared without further treatment. A case showing this clearly was that of Baby "A," aged 6 days when admitted to the hospital. The mother of this infant died two days after its birth. The cause of death in her case was given as pneumonia, but her blood was not examined. The infant was sent to the hospital with a diagnosis of pneumonia. The physical examination being negative, a blood examination was made and the specimen was shown to contain numerous estivo-autumnal parasites. One-sixth of a grain of atabrine and 1-/24 of a grain of plasmochin were given daily for five days. The fever disappeared at the end of the fourth day. The infant began to gain weight and was in very good condition from this time. Daily blood examinations showed the presence of parasites until the fourteenth day. The infant was discharged; he has returned several times since for examination; the blood has been negative and the physical condition remains normal. There has been no further treatment. Where possible all of our cases of treated malaria were followed for a period of one year.

Comparing this series with a series of several years before where quinine was used exclusively, we found that the number of relapses were fewer with atabrine and plasmochin treatment than under the older form where quinine was used.

As to the toxicity of the drug, the only symptoms seen resulting from atabrine in our series were, first, occasionally the patient complained of some abdominal pain, though this was rare. A more common symptom was the yellow discoloration of the skin which has in some instances lasted for several weeks. This mani-

festation we now all realize is only a dye and has no reference to toxicity.

We have used atabrine intramuscularly and intravenously with good results. In several instances it was used in hemoglobinuria with no toxic manifestations. It has also been employed in cases showing symptoms of cerebral malaria and no other drug has seemed to clear up the condition so quickly and so effectively. Several cases in our series died where atabrine was used where the chief manifestations shown before death were those of cerebral malaria, and the findings indicated that malaria was the cause of death.

As to the toxicity of plasmochin, we encountered more difficulty. Abdominal pain in some instances was quite severe and ceased when the drug was stopped. Belladonna, or atropine, given just before the dose of plasmochin in many instances allowed us to continue the drug without abdominal symptoms. Cyanosis was seen in several cases after plasmochin. Occasionally this was quite severe and lasted for days or even weeks. This severe form of cyanosis was particularly observed in those individuals having an allergic background. When we first began the use of plasmochin we combined it with quinine. The action of the two drugs appeared to be synergistic, but we did not believe we were obtaining sufficient benefits from the quinine to continue its usage. Neither Dr. McElroy nor I have seen any of the severe effects from the use of atabrine and plasmochin which were reported by Dr. Robert; nor have I been able to find in the literature evidence of death in a single instance as the result of toxicity of these drugs.

Our experience over a three-year period would lead us to believe that in atabrine we have a drug superior to quinine in the treatment of the asexual form of parasite as well as the sexual in the tertian variety. We believe that plasmochin is necessary to destroy the sexual form of parasite in the estivo-autumnal variety. The carrier in the estivo-autumnal type can be eradicated more effectively by the use of plasmochin than by the use of quinine. Quinine is a drug that has been used and proven of value in the treatment of malaria for many years, but I feel justified in stating that atabrine and plasmochin, at least to us, have proven of equal if not of more value in the treatment of malaria and that these drugs are not dangerous when their use is carefully supervised by a physician and they are given in the proper dosage.

Dr. Robert (closing).—I am indebted to Dr. Mitchell not only for his discussion, but also for material aid given in personal communications while this paper was in the writing. It was with a great deal of interest that I listened to Dr. Mitchell's paper in San Antonio last year and I resolved to try atabrine and plasmochin again and use the doses recommended by him. I did use these drugs again and spent many sleepless nights repenting and working on cyanotic babies.

The series reported by Dr. Mitchell was from the Memphis General Hospital and not from his private practice. If patients went bad no doubt there were interns and residents to work on them. Unfortunately I have not access to a charity institution and all patients treated by me are from my private practice. When medicine given by the physician makes a baby show even some of the symptoms mentioned by Dr. Mitchell, the parents will make said physician "sweat blood."

I wish to congratulate Dr. Mitchell not only upon the excellent results he has obtained with atabrine and plasmochin, but also upon the fact that he is one of the pioneers in this field. If he and others continue their experiments we shall have a safe dosage of these drugs for infants at some time in the future. I still contend that, although plasmochin is a wonderful drug, the dosage has not been standardized for infants, and until that has been done I am sticking to quinine.

I am sorry that some comment was not made about my "malarial pyelitis."

FACTORS CONCERNED IN MALARIA CONTROL BY DRUG TREATMENT*

By L. L. WILLIAMS, JR., M.D.†
Washington, District of Columbia

In recent years there has been a renewed interest in attempts to control malaria through the wholesale administration of drugs. Quinine, atabrine, plasmochin and various combinations of these drugs have been used, followed by reports of success and failure from all parts of the world. In reviewing the literature on the subject it is apparent that many of the opposing conclusions are based on clinical observations made only during an epidemic rise or a post-epidemic fall in the general malaria rate. Controlled experiments covering a long period of time are few.

The response to anti-malaria therapy varies tremendously between different races, between individuals of the same race, is unequal between the species of malarial plasmodia, and even varies between different strains of the same species. With these complex factors in mind, it seems timely to weigh the value of a program designed to control malaria rates through drug administration.

Control of malaria depends upon breaking the malaria cycle at some point. The most successful method is preventing production of *Anopheles*, but it is often the most expensive. In rural areas drug distribution is easier and seems far more economical, hence attractive. However, the response comes slowly and the effectiveness of the method is hard to measure. Therefore, it is natural that drug control should have been tried often; yet seldom has its effect been accurately gauged.

In attempting to control the infection rate among the population by drug administration the following factors must be considered:

(1) Finding the infected individuals;

(2) Curing the infection;

(3) Preventing relapses (or preventing carriers from infecting mosquitoes); and

*Chairman's Address, National Malaria Committee (Conference on Malaria), meeting conjointly with Southern Medical Association, Twenty-Ninth Annual Meeting, St. Louis, Missouri, November 19-22, 1935.

†Senior Surgeon, U. S. Public Health Service.

(4) Preventing the importation of new cases.

In endemic areas in very malarious countries spleen rates may be as high as 98 per cent. Under these circumstances the discovery of all infected individuals is easy and inexpensive. However, drug control is not feasible in such areas for, as pointed out by Christophers,[1] malaria control under such circumstances must be sure, else endemic malaria becomes epidemic with a high death rate. In sub-tropical countries, particularly in the United States, where sufficient treatment is taken to render the spleen rate an unsure method of finding infections, discovery of all malaria carriers is very difficult and expensive. Reports of physicians are insufficient, for it is estimated that less than one out of ten infected individuals seeks medical care. History indices as taken in the United States have shown such wide variations from blood indices as to render this method of case-finding useless. The best method we have today is the examination of thick blood films. This is not an economic procedure, for it is doubtful whether films can be taken and examined at a cost as low as 5 cents a slide. Even the thick film examination of a whole population does not reveal all the infected persons. A series carried out by Barber[2] shows that, commencing with a known 100 per cent infection, subsequent monthly examinations were not positive in more than 49 per cent of the cases and were as low as 27 per cent, yet each negative case was subsequently positive within a period of five months. In a group of Panama banana plantations where malaria rates were high, Barber, Komp and Newman[3] found:

"Among 407 positive specimens, which include some examinations not appearing in the tables, we found the following percentage incidence of type of parasites: estivo-autumnal, 82.3; benign tertian, 10.8; quartan, 6.8. In the same group of positives, 28.0 per cent showed heavier infections; that is, at the rate of one or more parasites per thick-film field. We resurveyed one camp, Margarita, after an interval of 19 days. The results give some idea of the proportion of parasite-carriers which may be missed in a single survey. In the second survey, positives appeared among persons previously negative in about the same proportion as among those previously positive (39 per cent and 43 per cent, respectively). The reexamination raised the percentage positive of the camp from 46.6 to 61.3, although only 70 per cent of those negative in the first examination appeared for reexamination. Such results show the inadequacy of a single survey as a basis for the treatment of a group. Where a single survey gives a rate as high as 46 per cent, as it did in this camp, it may be fairly presumed that all or nearly all of the population is infected."

In order to find all positive cases it would seem necessary to take an index of the whole population each month for almost half a year. Therefore, one can hardly expect an economic method of case finding to discover much over half of the infections in those localities where malaria rates are not excessive.

Once found, can the cases be quickly cured so that they will not become a source of infection to the mosquito? Drugs may be tried for three different purposes: preventing infection from developing in the human; preventing development of sporozoites in the mosquito; or sterilizing the parasites in the human carrier. It is almost axiomatic to state that "prophylactic" quinine, though successful in controlling clinical attacks, does not stop infection of the individual. Although there is some evidence that one of the synthetic drugs (atabrine) may yet be made more effective than quinine, to date it has succeeded only in prolonging the incubation period greatly in hospital experiments. In the field, use of this drug has not prevented infections with malaria.

Barber, Komp and Newman[4] demonstrated that minute doses of plasmochin had power to prevent the development of the sporogenous cycle in the mosquito. Later, Whitmore[5] was unable always to prevent this development with such small doses. Clark and Komp,[6] in a well conducted field experiment with the same drug in Panama villages, did not note any reduction in the sporozoite rate in the wild mosquito and were also unable to reduce the infection rate among the population. Recently, Sweet and Rao[7] attempted this type of control, using plasmochin and quinine once a week among the civil population where there was no compulsion to take the drug. They were never able to induce over 40 per cent of the total population to take the drug and in some weeks the percentage was as low as 8. The trial was unsuccessful. In an official village they were able to induce at least 51 per cent and sometimes as much as 87 per cent of the population to take the drug. Reduction of malaria was not very great and the record does not indicate that it was entirely due to the drug. Even if successful, the use of this drug is not a very safe procedure. It is so toxic that it should be administered only to those under medical supervision. Its use, therefore, becomes uneconomical and impractical.

Plasmochin effects only the gametocytes of *P. falciparum*. Quinine is a gametocide in benign tertian and quartan malaria, but there is no evidence that any quinine campaign has effectively reduced the sporozoite rate among the mosquitoes. In spite of their gametocidal action it seems apparent that none of these drugs entirely prevents the production of new gametocytes. From the experience of LePrince[8] in Panama it is known that it is possible to control malaria by eliminating infective mosquitoes. The work consisted in the mechanical daily destruction of all engorged *Anopheles* found within the houses. His success was secured by mechanical means, but there is no evidence that similar success has followed drug administration where a drug was administered to carriers to render gametocytes uninfective to the mosquito.

After an exhaustive review of the literature, the Malaria Commission of the League of Nations[9] comes to the discouraging conclusion that:

"(1) There is not at our disposal any drug, or any combination of drugs, which can be guaranteed to sterilize all the parasites in the human host and so to prevent the possibility of relapse."

"(2) For this reason no good purpose is served by endeavoring to bring about sterilization of all the parasites during the primary attack."

"(3) In nature, relapses cease to occur when the defensive mechanism of the human host has acquired sufficient power to overcome the fever and other clinical symptoms which the parasites cause in non-immune persons. The frequency and severity of relapses are dependent chiefly on the amount of defensive power which the infected person possesses naturally or acquires as a result of previous attacks. A scientific method of preventing relapses should be based on this knowledge or should take this knowledge into account by allowing an infected person to acquire as much defensive power as possible. Persons who are treated with large doses of quinine or other specific drug at the first onset of fever in their primary attack and in each relapse get no opportunity of acquiring sufficient defensive power to prevent relapses. Persons who are so treated usually relapse every month for a very long period. During the primary attack, it may not be safe to abstain for a day or two from giving a specific drug, but it is quite safe to do so in the first and subsequent relapse."

"(4) Thus, in a scientific system for the prevention of relapses, no attempt is made to give 'treatment for the prevention of relapses' during the primary attack. One waits until the first recrudescence and then uses the specific remedies in such a way that they will assist, rather than hinder, the development of the patient's natural defensive forces. By repeating this plan with the same watchfulness during the second recrudescence (using the specific drug at a later period and more sparingly than in the first recrudescence) and again, if necessary, during a third recrudescence, it happens, in most cases, that the patient becomes fortified or premunized against the disease to the extent that he not only ceases to suffer from relapses, but fails to have an attack when he is reinfected."

"(5) In the Commission's view, an endeavor to follow that plan should be made for the prevention of relapses of benign tertian and quartan fever. But they consider that, for preventing relapses of malignant tertian fever, it is justifiable to endeavor to sterilize all the parasites by specific drug therapy during the first recrudescence. For this disease the primary attack should be cured by a five or seven days' course of treatment with quinine or with atabrine and, if the patient has a recrudescence, this should be treated with a therapeutic course of five or seven days, but using the specific drug which was not used in the primary attack. If treatment during the first recrudescence is not successful in preventing relapses, therapeutic treatment of the third recrudescence should be delayed as long as possible in order to permit the patient to acquire some defensive power."

In other words, the Commission concludes that the ultimate sterilization of parasites in carriers depends more on the defensive mechanism of the body than it does on drug therapy. If this be so, then the best method of drug administration would allow much mosquito infection.

Sinton[10] disagrees with the view of the Commission. He claims a combination of quinine and plasmochin is an effective agent which greatly reduced malaria relapses. He quotes the works of himself and Smith and Pottinger, also observations of Jarvis, Manifold and Dixon. The treatment they prescribed consisted in 1.3 grams of quinine sulphate in solution with 0.03 to 0.06 grams of plasmochin daily for from four to twenty-one days. They claim that under this treatment relapse rates varied only from 4.1 to 11.3 per cent. These are remarkably low relapse rates. However, these were either hospital cases under the best of conditions, or else troops under discipline. This is the most hopeful treatment yet tested, and though it is not yet proven in the field it merits further research.

The fourth factor in attempting control of malaria by drugs, the importation of new cases of malaria, can hardly be eliminated at the present day with our easy transportation and modern habit of travel. Reduction of malaria infection among the population greatly lowers its tolerance to the disease and, as a natural consequence, importation of new infections should result in epidemics of malaria. In the United States where, through natural causes, the malarious area has been shrinking southward for many years, epidemics appear at intervals in territory recently freed from the disease. During the past two years such epidemics have occurred in the States of New Jersey, Ohio and Michigan, and in the mountainous portions of such recognized malarious states as Virginia, North Carolina and Georgia. If such an epidemic return can occur among populations where malaria disappeared because the area was no longer suitable for its continuation, then surely it will return even more quickly and again become endemic if it were driven from its normal habitat by means of drug administration. The campaign would have to be repeated again and again, amounting almost to a constant wholesale drug administration in an entire population.

It would seem that one cannot expect a very great measure of success in attempting to control the malaria rate by administering to the population any of the drugs now known, except that the case for the combination of quinine and plasmochin is not closed.

In the expectation of further experimentation with drug control, we must emphasize again the necessity of prolonging an experiment for a sufficient time to include the entire cycle of malaria in the population studied. This point will be illustrated in detail in a paper by Komp and Clark[11] which follows this presentation. In the light of conclusions which may be drawn from the Panama work of Komp and Clark,[12] covering five consecutive years, it is possible that only one year of observation may lead to faulty deductions unless the exact cycle of malaria is known in each section and is taken into consideration. They happened to start their experiments with quinine, plasmochin, and atabrine in Panama when the trend of malaria was downward. At first control by drugs seemed successful, but in ensuing years drugs were powerless to prevent the sharp rises which occurred when the trend of malaria was upward.

In a population of nearly 800 in five villages a monthly thick film blood index was taken of about 500

persons. These slides were examined immediately and every person whose blood showed malarial parasites was given treatment. Each treated case was reexamined and if not found parasite-free was treated until parasites had disappeared from the peripheral circulation.

After charting the monthly rates for five consecutive years, they could see not only the seasonal rises and falls, but also that there were cyclic waves each of two years' duration. The sharp upward trend of each wave and its prolonged decline more accurately pictures the natural ebb and flow of malaria in the population than does any one, two or more of the seasonal fluctuations.

The first attempt to control the malaria infection rate with drugs was started near the end of a cyclic wave when the trend was downward. The apparent effect on seasonal fluctuations was such as to induce the belief that the experiment was successful in lowering the infection rate. When it was continued into the next wave where the trend was upward, the experiment was manifestly a failure.

In the last experiment (quinine plus plasmochin in one group and atabrine followed by plasmochin in another) control of malaria by means of drugs seemed very hopeful throughout the entire year of study, because it also was started at the beginning of a downward trend. However, hopes were completely dashed as the subsequent upward trend brought very high rates in all villages.

The introduction of good treatment among a native population in Panama promoted their well-being, reduced the number of actively sick persons, and accelerated the natural decline in the parasite rate when the trend of malaria was downward. When the trend was upward, all drugs tested were powerless to control the infection rate. From Komp and Clark's experience it is evident that experiments designed to test the efficacy of any drug to control malaria must be continued through a sufficient length of time to cover a complete cycle of the disease.

It may be concluded from the above discussions that malaria control through the administration of drugs is not a hopeful procedure. Successful in reducing clinical attacks of malaria, it offers little hope for controlling the malaria rate, is difficult to apply, and is uneconomical.

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TREATMENT OF MALARIA BY THE SHORT COURSE METHOD*

By J. P. SANDERS, A.B., M.A., M.D.
Caspania, Louisiana

The treatment of malaria by the short course method, of course, is not new. It dates back, probably, before the time when Canizares, the Spanish Corregidor of Loxa, in 1630 took bark for his intermittent fever and was cured. The Indians probably used it when they drank the bitter waters from lakes where cinchona trees had fallen. One drink was probably all that most of them took and many were cured of their fevers.

The Jesuit priests gave 8 grams of the bark, equivalent to about 12 grains of cinchona alkaloid, just before chill time and repeated the dose till the patient recovered. Sydenham[1] (1624-1689) prescribed 32 grams of the powdered bark (equivalent to about 48 grains of the alkaloids of cinchona) in 2 pounds of red wine. This he divided in twelve doses and gave every 4 hours, starting immediately after the paroxysm had subsided. He repeated this treatment in 8 to 14 days according to the type of fever and repeated this several times if the patient had long had the fever or was debilitated. Trousseau found this method preferable to that used by the Jesuit priests, namely, the one-course treatment.

In 1866-8 the Madras Chinchona Commission,[1] working in southern India in areas notedly malarious, reported a series of 3,617 cases treated with quinine, quinidine, cinchonine and cinchonidine in order to de-

*Read before National Malaria Committee (Conference on Malaria), meeting conjointly with Southern Medical Association, Twenty-Ninth Annual Meeting, St. Louis, Missouri, November 19-22, 1935.

termine their relative efficacy. They reported a high percentage of "cures" from the administration of a single 10-grain dose of the alkaloid and that the four alkaloids were about of equal value in the treatment of malaria.

Recently, the medical literature has been full of all sorts of short-course methods. Sanders and Dawson,[2] in 1932, reported a comparison of quinidine with quinine, using a single daily 10-grain dose for 4 days with surprisingly good results in both. Collins,[3] in July, 1934, reported a series of cases treated with a single daily one-gram dose for 3 to 4 days with good results. Dawson and others[4] recently reported a short series of cases, seven of which are included in this report, treated with the rare hydro-alkaloids, hydrocinchonine and hydrocinchonidine. They used the single daily 10-grain dose for only 4 days and demonstrated "definite strong anti-malarial properties." Hill and Olavarria[5] have just reported a series of cases treated over a three-year period by a single 1-gram dose of quinine sulphate for 4 days. Their results are most gratifying. Of 234 new benign tertian infections only 15 per cent recurred the same year and only 35 per cent recurred the following year, giving a percentage of "cures" for the season of 85 and for the year 65. Of the recurrences, the results were not so good. Of 231 spring recurrences of benign tertian infections, 60 per cent recrudesced following treatment; of the 56 malignant tertian infections, 90 per cent recrudesced following this short course.

De Lee,[13] working in Charity Hospital, Shreveport, Louisiana, is doing some very interesting work in cases of malaria that come in in a comatose condition. In the past two years he has treated about fifty cases of cerebral malaria with large doses of quinine dihydrochloride given as an infusion in normal saline and 5 per cent glucose. He gives from 15 to 45 grains in 500 to 2,000 c. c. solution in from 12 to 24 hours. The patient usually comes out of his coma in from 3 to 12 hours. He has lost no patients so treated. He gives the infusion at the rate of about 80 drops per minute.

Cinchonine and cinchonidine and hydroquinine[1 6] have all been shown to have high anti-malaria value both by the short and long course methods.

Atabrine was first tested clinically in 1932 by Sioli.[7] He found the optimum value in daily doses of 4½ grains (divided in 3 doses) for 5 consecutive days. Many other investigators reported excellent results. Hoops[8] writes that

"the production of 'atebrin,' a drug far more effective than quinine in that it apparently eradicates the malaria parasite as a rule after only 5 days' treatment, is 'an event in the history of tropical medicine."

Thonnard-Newman and Le Doux,[9] working in the United Fruit Company Hospital, Santa Marta, Colombia, reported excellent results in 75 cases of malaria. No irritation to the liver or kidneys was observed. All reported the yellowing of the skin due to deposits of the drug under the skin. The lay press has been very commendatory toward the drug itself as a "cure" for malaria. But Komp and Clark,[10] in a report before this Committee last year, were unable materially to lessen the incidence of malaria in Panama by the use of atabrine. Dawson and Gingrich[11] considered it a dangerous drug given intravenously and suggested that it be given only in an emergency.

Table 1

TOTAL CASES TREATED OVER 6-YEAR PERIOD

	1930	1931	1932	1933	1934	1935	Total
Quinidine	39	65	130	502	311	302	1349
Quinine		61				20	81
Cinchonine				9		13	22
Cinchonidine				17		9	26
Hydroquinine					3	4	7
Hydrocinchonine and hydrocinchonidine	7						7
Atabrine			1	29	9	16	55
Total							1547

PLAN OF TREATMENT

In this report are included 1,547 cases of malaria treated during the past six years, 1930 to 1935, inclusive, with 8 different drugs, all of the cinchona group except atabrine. They represent all the cases of malaria that I have treated in the past six years (except that I started late in the season of 1930) in my general practice. In the beginning I kept up with them, taking blood smears at regular intervals, but as the numbers increased this task became impossible and consequently these reports are largely clinical except for the first diagnosis, which is corroborated by a blood smear. However, it is a stable population, with little changing and if the patient gets sick again I know about it. The patients are largely Negroes and I have to depend on them, ignorant as many of them are, to administer the drug to themselves.

The course of treatment has been a four or five-day treatment, repeated only if the patient relapsed clinically or showed a positive blood smear. The cinchona alkaloids were all given as a single 10-grain daily dose for 4 days (a total of 40 grains of the sulphate or hydrochloride) until 2½ years ago, when the malaria condition became so acute because of a flood in the community that the course was changed to two 10-grain doses given night and morning for 2 days and then 10 grains for three more nights (a total of 70 grains). The atabrine was given as directed by the manufacturers, fifteen 1.5 grain tablets, taken one three times a day for 5 days. The cinchona alkaloids were administered, as the sulphate or hydrochloride, in 5-grain capsules, two to the dose.

Table 2

CASES TREATED WITH QUINIDINE IN 1935

Age	0-10	10-20	20-30	30-40	40-50	Above 50	Total
Benign tertian	20	24	35	14	10	21	124
Malignant tertian	12	20	21	1	4	8	66
Negative	11	26	27	18	13	17	112
Totals	43	70	83	33	27	46	302

Table 3

TOTAL CASES TREATED WITH QUINIDINE

	1930	1931	1932	1933	1934	1935	Grand Total
Benign tertian	12	21	27	231	129	124	544
Malignant	5	20	45	109	64	66	309
Negative	22	24	58	162	118	112	496
Totals	39	65	130	502	311	302	1349

QUINIDINE

Before this Association last fall the author[12] reported 1,047 cases of malaria treated over a five-year period with quinidine. This report includes those cases and 302 cases treated with quinidine this year, making a grand total of 1,349 cases of malaria treated during the six-year period.

Table 4

PATIENTS SHOWING RELAPSES (OR NEW INFECTIONS) IN SUCCEEDING YEARS

Year	Total Treated	1931 No.	1931 Per Ct.	1932 No.	1932 Per Ct.	1933 No.	1933 Per Ct.	1934 No.	1934 Per Ct.	1935 No.	1935 Per Ct.
1930	39	4/35	11.4	5/33	15.1	11/32	34.4	4/32	12.5	9/30	30
1931	65			16/56	28.6	13/43	25.6	11/40	27.5	8/31	26
1932	130					27/103	26.2	14/95	14.7	15/69	21.7
1933	502							78/400	19.5	52/241	21.6
1934	311									56/211	26.5
Average		140/582	24								

Table 5

LIST AND PERCENTAGES OF "CURES" IN SUBSEQUENT YEARS

PATIENTS TREATED IN 1930

	1931 No.	1931 Per Ct.	1932 No.	1932 Per Ct.	1933 No.	1933 Per Ct.	1934 No.	1934 Per Ct.	1935 No.	1935 Per Ct.
Benign tertian	8/11	72	9/11	81	6/11	54.5	10/11	91	8/12	67
Malignant tertian	3/4	75	2/4	50	2/4	50	2/4	50	1/4	25
Negative	17/17	100	15/16	93	11/15	73	14/15	93	12/14	84
Totals	28/32	87.5	26/31	83.8	19/30	63.3	26/30	86.7	21/30	70

PATIENTS TREATED IN 1931

Benign tertian	12/20	60	13/18	73	10/15	67	9/12	75
Malignant tertian	12/15	80	6/8	75	6/8	75	7/8	87.5
Negative	16/21	76	11/17	67	12/16	75	7/11	63.3
Totals	40/56	71	30/43	70	28/39	71	23/31	77.7

PATIENTS TREATED IN 1932

Benign tertian	14/18	78	12/16	75	7/13	54
Malignant tertian	25/37	67	28/35	80	21/24	87.5
Negative	35/48	73	37/44	84	27/29	93
Total	74/103	71.8	77/95	81	55/66	83.3

PATIENTS TREATED IN 1933

Benign tertian	135/181	75	80/105	76
Malignant tertian	42/86	49	26/47	55.3
Negative	106/116	91	67/90	74.4
Totals	283/383	73.8	173/242	71.5

PATIENTS TREATED IN 1934

Benign tertian	57/85	67
Malignant tertian	41/52	80
Negative	58/81	71.6
Totals	156/218	71.6

Table 6

TOTAL CURES AFTER INITIAL TREATMENT WITH QUINIDINE

	For One Year No.	For One Year Per Ct.	For Two Years No.	For Two Years Per Ct.	For Three Years No.	For Three Years Per Ct.	For Four Years No.	For Four Years Per Ct.	For Five Years No.	For Five Years Per Ct.
Benign tertian	226/315	71.7	114/150	76	23/39	59	19/23	82.6	8/12	67
Malignant tertian	123/194	63.4	62/94	66	29/36	80	9/12	75	1/4	25
Negative	232/283	82	129/167	77.2	50/60	83	21/26	80.7	12/14	84
Total	581/792	73.5	305/411	74.2	102/131	77.8	49/61	80	21/30	70

In Table 2, the patients treated in 1935 have been grouped by ages. In keeping with the findings of others, malaria is most prevalent during the first three decades, 196 out of 302 cases. But the table indicates at least one peculiarity, the decided dropping off of malignant tertian infections after the third decade to 13 out of a total of 66, especially between the ages of 30 and 40, when there was only one case.

Table 3 shows the total number treated, grouped by years and by types of infection. Table 4 shows the number of patients relapsing in the succeeding years and the number of patients followed, thereby giving the percentge of relapses in the first, second, third, fourth and fifth years. The average relapse rate for the whole group is 24 per cent, leaving approximately 76 per cent "cures." These "cures," that is, those that did not relapse the following year, are listed in Table 5. As in the previous paper, the author has attempted to show what happens to patients in subsequent years. Table 6 gives the one-year, two-year, three-year, four-year and five-year cures. These results vary very little (from 70 to 80 per cent) and the larger the group gets the more nearly it seems to approach the 75 per cent mark.

Thirty-eight cases of pregnancy in all stages tolerated quinidine without ill effects. Ten cases of hematuria or hemoglobinuria were not affected by the drug. As previously reported,[12] 3 cases showed a definite idiosyncrasy to quinidine. A patient with an estivo-autumnal infection finished his course of quinidine one night and the next afternoon began to pass pure red blood (red cells in urine). He was put on atabrine and appropriate treatment for the hematuria and soon cleared up. He was clinically well (except weak and anemic) at the time his hematuria began and a blood smear was negative for parasites.

Table 7

CASES TREATED WITH QUININE

Year	Benign Tertian	Malignant Tertian	Negative	Total
1931	30	13	18	61
1935	3	3	14	20
Total	33	16	32	81

In this series of 81 cases (Table 7) 61 cases were previously reported.[2] In that report, it was shown that 40 per cent of estivo-autumnal and 53 per cent of benign tertian infections were clinically well and blood smear negative for 100 days or more after having taken only 4 doses, 10 grains each of quinine sulphate. The fever subsided in about 4 days and the patient was clinically well in about ten. Of the 20 cases treated this year by the 5-day, 7-dose method, 2 had previously taken quinidine this season. Neither had relapsed after 45 days. Of the other 18, 2 did not become clinically well and a third relapsed in 2 weeks and the three were put on quinidine. They have been clinically well 25, 72 and 75 days, respectively. Nine of the others have been well now over a period of from 100 to 300 days. One other relapsed in about two months.

Table 8

CASES TREATED WITH HYDROQUININE

Benign tertian	3
Malignant tertian	3
Negative	1
Total	7

In this small group of seven cases, 3 treated last year and 4 this year, 2 cases (1 last year and 1 this) were little improved in about three days and were so sick that they were put on quinidine, though their blood smears were negative. They recovered promptly with quinidine. Another has been clinically well with negative blood smears for two seasons. Another treated last year remained well, but came down with the disease this year. The other 3 cases treated this year have remained clinnically well. One of the patients was a white woman, the first patient that I treated with quinidine in 1930, who had been malaria-free since that time, though constantly exposed to both benign and malignant tertian infections in her family.

Table 9

CASES TREATED WITH CINCHONINE

Year	Benign Tertian	Malignant Tertian	Negative	Total
1933	4	4	1	9
1935	3	5	5	13
Total	7	9	6	22

Table 10

CASES TREATED WITH CINCHONIDINE

Year	Benign Tertian	Malignant Tertian	Negative	Total
1933	8	4	5	17
1935	0	6	3	9
Total	8	10	8	26

This pair of dextro and levo-rotary isomers analogous to quinidine and quinine, respectively, were used in treating a total of 48 cases of malaria. Of the nine treated with cinchonine in 1933, 4 were followed in 1934 with one relapse; none relapsed in 1935. Of the 17 treated with cinchonidine, 14 were followed in 1934 and 13 in 1935. Two relapsed each year.

In the group of 13 treated this year with cinchonine, 3 had previously taken a course of quinidine, 3 quinine and 3 chill tonic. All are still clinically well, though no one has taken the treatment over 40 days ago. Similarly with cinchonidine. Two of the nine had taken quinidine, one quinine and one chill tonic. All are still clinically well, though none has taken the drug over 40 days.

Table 11

CASES TREATED WITH HYDROCINCHONINE AND HYDROCINCHONIDINE

	Hydrocinchonine	Hydrocinchonidine
Benign tertian	2	2
Malignant tertian	2	1
Total	4	3

These two alkaloids, previously reported,[4] were found to have definite and positive anti-malarial value in the four 10-grain doses. With hydrocinchonine all 4 cases were symptom-free within a week, one within six days. One relapsed clinically in 28 days and was put on quinidine, while 2 more became blood smear positive in 30 and 35 days, respectively, and were put on quinidine. The fourth remained clinically free the remainder of the season.

Of the 3 cases treated with hydrocinchonidine, one relapsed in 15 days and was given the second round of 4 doses of the same drug and remained clinically well the remainder of the year. Another relapsed in 23 days and was put on quinidine, while the third was clinically well with negative blood smears a year later.

Table 12

CASES TREATED WITH ATABRINE

Year	1932	1933	1934	1935	Totals
Benign tertian	1	19	7	2	29
Malignant tertian	0	11	2	10	23
Negative	0	0	0	4	4
Totals	1	30	9	16	56

In Table 12 I have listed by years and types the patients treated with atabrine. Of the 29 benign tertian infections one died of typhoid fever and one was so ill that two days after starting treatment she was changed to quinidine. Of the remaining 27 cases, 10 relapsed in from 6 to 45 days, making a percentage of 37. In the estivo-autumnal group (malignant tertian) of 23 cases, 4 were so sick on the second and third days that atabrine was discontinued and quinidine substituted, and the fifth had a positive blood smear on the fifth and felt so ill that quinidine was substituted. Of the remaining 18 cases 7 relapsed in 6 to 35 days, or a percentage of 36.8.

The first patient treated in this series, a Negro man, aged 50, had a benign tertian infection in 1932 and has remained clinically well with negative blood smear since that time, though living in the house where there are malaria patients every year.

One of this group, a well developed, husky Negro girl, 11 years old, with a malignant tertian infection, was put on atabrine and after taking three tablets (the adult dose) developed a definite psychosis of the depressive type. Her temperature was normal and she was not complaining of pain anywhere. She was put on quinidine and came out of the psychosis in about three days' time. Several physicians in Shreveport have complained of these reactions to atabrine, which usually come on after the whole course has been completed or after repeated courses. The mental symptoms remain from three days to six weeks, according to reports.

I had occasion to compare the clinical results of atabrine with quinidine on four patients in the same house, sick in two beds at the same time in the same room. All four were Negroes, three brothers and a sister, ranging in ages from 18 to 22 years. There was only about one degree difference in their four temperatures when I saw them, at 104-5° F. They all had a chill that day and blood smears from all were teeming with estivo-autumnal parasites. I gave the two in one bed, a boy and the girl, quinidine and the other two boys atabrine. Three days later I was called back. The girl was in the kitchen cooking and her bed mate was sitting on the porch singing. The two that were taking atabrine were both in bed, one with a temperature of 103.6°, complaining terribly, and the other with a temperature over 104° and delirious. Their hearts were fast and weak and they were so ill that I was afraid I would lose them. I put both on quinidine and in two days both were sitting up.

SUMMARY AND DISCUSSION

The author realizes the inadequacy of the number of patients treated, except for quinidine, to draw direct comparisons and conclusions as to the relative efficacy of the drugs used. But the cases studied and the number of drugs used do indicate a certain trend. From an experience with 1,349 cases treated with quinidine by the short course method over a six-year period, the author believes he has proven what that drug will do. A physician who sees patients with clinical malaria, without a blood smear diagnosis, usually may know that 3 out of 4 (or about 75 per cent) will stay clinically well after quinidine treatment throughout the rest of the season and the next year, except for the few that relapse and have to take the second and third courses. But if a blood smear reveals a malignant tertian infection, then only 3 out of 5 (or about 60 per cent) usually will remain well after quinidine treatment. About 85 per cent of those clinically malaria, but negative for parasites in the blood, will remain well. The short course of quinidine has controlled the acute attack in every case. No cinchonism has ever appeared from quinidine administration.

With quinine, the period of recovery is a little longer, but the acute attack will be controlled usually by the short course. Relapses will occur in about 25 to 40 per cent, more of course in the estivo-autumnal type.

The action of hydroquinine is definite and rapid in most cases, though two cases were put on quinidine on the third day. The other 5 hydroquinine treated cases remained well throughout the season, a percentage of "cures" of 71.

Cinchonine and cinchonidine seem to relieve the acute symptoms promptly. Of those treated in 1933 and studied through 1934 and 1935, from 75 to 85 per cent remained well the next year. This seems a little high and is probably so because only a small number were followed.

Hydrocinchonine and hydrocinchonidine seemed to be

of about equal value. Two out of the 7 remained well for the year, a "cure" rate of 29 per cent, while the rest relapsed in five weeks. All cases were clinically well after taking 4 doses.

Atabrine seems of about equal value in the two groups (benign tertian and malignant tertian) in preventing relapses. About 37 per cent of each group relapsed within 6 weeks (6 to 45 days), leaving the remaining 63 per cent "cured." In the benign tertian group the patients tolerated the drug well and recovered promptly. But among the malignant tertians about 17 per cent (4/23) will respond so slowly and become so ill that continuance of the drug alone seems inadvisable. Occasionally, mental symptoms develop that are troublesome. In the whole series only 2 patients died: one after taking 3 doses of quinidine and the other after taking four.

The country where this work was carried on (Louisiana) is moderately malarious, but not extremely so, as is seen in other parts of the world. For the most part the people are well nourished and have been taking quinine for a generation or so. These two factors have to be considered in studying the response of any drug to a disease so devastating as malaria. The individual resistance plays a big part in the patient's recovery. For these reasons it would probably be easy to duplicate these results here in the United States, but difficult in India.

CONCLUSIONS

(1) Quinidine is in my experience definitely superior in controlling the acute attack of malaria and slightly superior in preventing relapses.

(2) Quinine, cinchonine and cinchonidine are of about equal value both in relieving the acute attack and in preventing relapses.

(3) The hydro-alkaloids, hydroquinine, hydrocinchonine and hydrocinchonidine, are of definite anti-malarial value and may be used in the treatment of malaria.

(4) Atabrine is of definite value in malaria; is an addition to our malarial armamentarium, but probably a little overrated as a "cure all" for malaria.

(5) Though we may have many drugs now that will "cure" malaria, none has been found that will rid the blood stream of all the plasmodia, that is cure that last 25 to 40 per cent.

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DISCUSSION (*Abstract*)

Dr. W. T. Dawson, Galveston, Tex.—Some years ago "Grove's chill tonic" had on the label a note to the effect that it contained quinidine and cinchonidine. The reason for selection of these in preference to quinine is possibly that this preparation contains small crystals of base (alkaloid) to be suspended by shaking before each dose, and quinine does not really give such crystals, being generally in a fine powder; or it may be simply a question of price differential; ordinarily quinidine costs more than quinine, but in order to prevent several tons of quinidine from accumulating every year it is possible that the quinidine production may be cleared up by making a low price on it in large bulk. These things are of course not of great scientific interest, the main point being that the minor cinchona bases are extensively used in chill tonics for the southern United States, or, one might more fearlessly say, have been so used.

On the short course method of treatment of malaria with quinine the most important studies, apart from the work of the Texas-Louisiana group, including especially Dr. Sanders, in this country, seem to me to be that reported in the League of Nations Quarterly Bulletin, Health Organization (2:197-300, 1933); that of Dr. R. K. Collins (Amer. Jour. Trop. Med., 14:329, 1934); and of R. B. Hill and Jose Olivarria (J.A.M.A., 104: 2329, 1934).

H. G. Bevil (Amer. Jour. Trop. Med., 12:473, 1932) used hydroquinidine in short course treatment of malaria.

Dr. Sanders was really the first of recent workers to report results with short courses of quinidine so far as I know anywhere in the world. In 1931 (J.A.M.A., 97:850), he reported treatment of a patient with malaria who had an acquired anaphylactoid reaction to quinine. He compared short courses of quinine and quinidine in a paper in which I was by his courtesy allowed to figure as joint author (J.A.M.A., 99:1773-1777, 1932) so that he seems to be well up in the procession of observers of effects of short courses of quinine and other cinchona bases in malaria. Of course the Madras Chinchona Commission of 1866-68 employed one to four-day treatments very extensively, and the early workers with the bark in the Seventeenth and Eighteenth Centuries used a variety of schemes.

RECENT RESEARCH ON PROPHYLAXIS AND TREATMENT OF MALARIA*

REPORT FOR 1935

By HERBERT C. CLARK, M.D.
Panama, Republic of Panama

As a member of the Committee on Medical Research, I have been requested by the Chairman to prepare a summary of prophylaxis and treatment of malaria during the year ending September 1, 1935. Undoubtedly many of the present year's records will not be included in this summary, since we have not access to all of the world's literature filed during this period of time and we hope the authors of papers not abstracted will understand why they do not appear in this summary. It will also be taken for granted that the membership of the National Malaria Committee and the readers of this report are well acquainted with the efficacy of quinine and the various methods of using it as an anti-malaria drug. It is still our number one drug for the masses. However, the small space allotted for this review will be given to the new drugs that have been given field trials.

Studies in Untreated Malaria.—It seems worth while, at the very beginning, to record a brief statement from Lowe,[1] who calls our attention to the fact that the relation of the numbers of parasites to the course of untreated fever is not the same in benign tertian and subtertian. The parasite counts made by him ranged from 20 to 202,000 per cu. mm. In benign tertian malaria, a minimum count of 500 parasites per cu. mm. is usually necessary to cause fever. On an average, only some 20 per cent of the young trophozoites reach maturity.

In subtertian malaria a count of 600 to 1,500 parasites is usually necessary to cause fever. The increase or decrease in the parasite count is not necessarily followed by an increase or decrease in the fever of subtertian malaria, but in benign tertian the fever generally rises and falls with the number of parasites. The author considers that the destruction of parasites occurs in two ways: (1) by lysis or phagocytosis of free merozoites; (2) by ingestion of infected red cells by the reticulo-endothelial system. It seems to be more or less generally held that our anti-malarial drugs do not kill parasites by direct action, but they simply stimulate the reticulo-endothelial system. If this be true, then the possibility of blocking this system by over treatment with any drug must be given our consideration.

Kritschewski and Demidowa[2] reach the conclusion that the therapeutic activity of anti-malarial drugs is greatly lowered by blocking the reticulo-endothelial system with trypan blue. Others experimentally produce the same result with india ink. May we not also induce the same condition by the overdose of any of the anti-malarial drugs?

NEW DRUGS

White and Adhikari[3] report that a single course of quinine and plasmochin given at the beginning of the malaria season to all children living in an area under anopheline control caused no permanent improvement.

Green[4] considers that it will be necessary to have the results of prolonged and well conducted experiments before forming any opinion on the use of atabrine as a clinical prophylactic. He does not think that it would be safe to give subcurative doses of atabrine, say 0.1 gram daily, over long periods, because of the possible cumulative effects. He reports 4 per cent relapse under atabrine treatment and 38 per cent relapse under quinine treatment. His period of observation, however, was only 27 days for atabrine and 18 days for quinine.

Manson-Bahr,[5] in discussing the prognosis in malarial infection, states very definitely that relapses in subtertian malaria can be entirely prevented by atabrine. The life span of the benign tertian parasite is given by him as 3¼ years, that of subtertian at about nine months and of quartan at six years. We like the conclusions of Williams and Bhattacharyya,[6] who regard atabrine as a more suitable drug for those who can afford it, but consider that it cannot replace quinine in general use in a poor country like India. The usual curative course of quinine on the tea gardens consists of 20 grains daily for seven days. The small reduction of malaria which followed prophylactic treatment with atabrine and plasmochin was not sufficiently satisfactory to compensate for the expense incurred.

TOXIC EFFECT OF THE NEW DRUGS

Chopra and Chandhuri[7] have recorded some observations on the toxicity of synthetic anti-malarial remedies and they conclude that plasmochin and atabrine should not be given together and that neither plasmochin nor atabrine should be used for prolonged periods for prophylactic purpose. No one should be allowed these drugs except under direct medical supervision. Kingsbury[8] reports seven cases of psychosis following the use of atabrine in cases of malaria. These occurred among several thousands of cases of malaria treated with atabrine. Perhaps it would be well for us to consider other causes for these few cases. They may have been the direct result of malaria. Furthermore, the incidence of a psychosis due to other causes among that number of people should also be considered.

OTHER NEW DRUGS

Mosna[9] reports the use of "quinoplasmine" in malaria prophylaxis. He used an administration twice weekly of the drug (2 centigrams to adults with doses proportionately less for children) to the entire population of

*Read before National Malaria Committee (Conference on Malaria), meeting conjointly with Southern Medical Association, Twenty-Ninth Annual Meeting, St. Louis, Missouri, November 19-22. 1935.

771 in a community where malaria is endemic. This treatment extended over a period of about five months, May 18 to October 21. His results are tabulated as follows:

(1) A marked reduction in malaria incidence among the population in general.

(2) Marked reduction in incidence among those born during the year.

(3) Absence of infected anopheles throughout the period of experiment.

(4) Absence of symptoms of toxicity or intolerance of the drug.

Russel,[10] in his discussion of malaria and its control in the Philippines, offers some complimentary remarks on totaquina. He advocates the local cultivation of cinchona and the manufacture of totaquina. He believes there is a potential market in the Philippines alone for some 33 tons of totaquina annually, without competing at all with the quinine and synthetic products now imported. Totaquina is less bitter than quinine, has no bad effects and is equally efficacious. It would meet the need for an effective and much cheaper remedy. There would be a market for it in South China and, possibly, in the southern United States.

PERSONAL EXPERIENCE IN PANAMA

Komp and Clark[11] reported their fourth year's observations on malaria in Chagres River villages with reference to control with atabrine and plasmochin. No mosquito control nor house screening has been in use at any time during this period. Various combinations of anti-malarial drugs were used, including quinine sulphate alone or with plasmochin, and with atabrine alone or with plasmochin. None of the methods used was so successful as we had hoped in reducing the parasite rate. Monthly blood surveys over four years indicate the presence of cyclic variations in the malaria parasite rate extending over several years. If treatment of any sort happens to be given during the down-swing in rate success is almost sure to follow, but if it is given on an upswing in rate apparently nothing can stop the natural course of the cycle. The control towns show too little difference in parasite rates to warrant such methods of survey and drug control. There has been a very slow decline in town parasite rates over these years to a point where we thought only chronic cases and relapses accounted for most of the parasite index, but since the fourth year's report was made an epidemic of the disease has occurred that carried our rates to an average of about 30 per cent and many of these cases were in persons who had been on our negative list for a long time. This is all the proof we need to establish the fact that we did not control the oöcyst rate even over these five years of treatment efforts. From the standpoint of a commercial organization operating under such conditions we have no doubt that we have accomplished much good in the way of building up the general health of these villages. The number of chronic infections has been reduced and the people are now prompt in taking treatment when the disease shows actively, a business man's control, but not a scientific control. In our opinion, the question of preventing relapse, in any species of malaria, and the question of a drug to kill the gametocytes and sterilize the mosquito are confronting us almost as much as they were twenty years ago.

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RECENT RESEARCH UPON THE DIAGNOSIS OF MALARIA*

By WENDELL GINGRICH, Sc.D.†
Galveston, Texas

Discussion of Henry's melano-flocculation test continues to account for most of the recent publications relative to the diagnosis of malaria, although many papers treat of the clinical diagnosis of "pseudo-malarial" fevers due to infections of pneumococci, meningococci, *N. catarrhalis* and even conditions such as infant diarrheas, prostatic abscess, and so on, in relation to malaria. One author states that "pernicious types of malaria are more readily recognizable from physical signs than from blood studies" and classifies these types as (1) "algid," (2) "pneumonic or congestive . . . the diagnosis is made at autopsy," (3) "bilious," (4) "comatose," (5) "choleraic and dysenteric," (6) "hemorrhagic" (Coogle 1935). However, it is not my purpose to cover all the very interesting clinical notes on the diagnosis of malaria and I shall therefore limit the

*Read before National Malaria Committee (Conference on Malaria), meeting conjointly with Southern Medical Association, Twenty-Ninth Annual Meeting, St. Louis, Missouri, November 19-22, 1935.

†Department of Bacteriology and Preventive Medicine, University of Texas School of Medicine.

present discussion to literature which may be considered to be related in one way or another to research.

The status of the applicability of the melano-flocculation reaction to the diagnosis of malaria is about the same as it was a year ago. (For an introductory discussion of this test the reader is referred to the present writer's previous brief review). According to Chorine (1934) a negative reaction means the absence of malaria, but a positive test is only presumptive evidence of its presence. That the test is positive in frank malaria is reported by all investigators. It remains positive during and after treatment (6 to 60 days according to various authors) and it is positive in cases which are parasite-negative by microscopic examination, but may be presumed to be chronic malaria. However, it is also more or less regularly positive in typhus, kala-azar, Weil's disease (Dohnt 1934), hemolytic icterus (Lacour 1934), and spirochetosis of fowls (Trensz 1934) and is occasionally positive in syphilis, hemolytic streptococcic septicemia (Dohnt), anemias, cirrhosis of the liver, tuberculosis (Trensz 1934b and Chwatt 1934), etc. To eliminate these "false" or "anomalous" positives or "non-specific" reactions, Henry (1934) states that if flocculation occurs in a serum after it has been heated (55° C. for one-half hour) one knows that it is not "specific." Apparently a control with heated serum is necessary. Sinelnikow and associates (1935) advise previous heating of the sera at 54° C. for five minutes to eliminate the possibility of "non-specific" reactions. Inasmuch as the reaction very probably is due to the precipitation of a globulin it is difficult to accept these methods of excluding "anomalous" reactions with sera such as those of kala-azar patients in which the globulin content is very high. There is a practical precaution indicated by Chorine and Koechlin (1934), who studied the daily variation in the reaction with sera kept for ten days. Their work shows that a serum kept separated from the clot gave reactions in the form of a sinusoidal curve, whereas with a serum left in contact with the clot there is a steady, slow decline in titre. The test should therefore be made as soon as possible after the blood has been collected, and the serum should not be separated from the clot until needed.

Research upon the nature of the reaction in the recent publications turns upon the question as to whether the mechanisms of melano-flocculation and of "surfloculence" are essentially different or identical. "Surfloculence" is the term applied to precipitation (evidently of a globulin) in sera diluted with distilled water. Wiseman (1934) carried out a series of tests using the melanin of Grieg (see writer's previous review) and a parallel series using distilled water. He obtained identical results in both series and concluded that the two "phenomena are one and the same, the melanin merely adding a brown colour to the flocculation. . . . The precipitate in all probability is a globulin."

Chorine, Prudhomme and Koechlin (1934) collected sera from normal persons, syphilitics and malaria patients and carried out parallel "surfloculence" and melano-flocculation tests. They found that sera giving photometer readings less than 10 in distilled water gave negative Henry reactions; sera with readings of 10 to 25 gave doubtful tests; and sera with "surfloculence" readings above 25 gave positive melano-flocculation. Among sixty-six malarial sera, sixty gave photometer readings in "surfloculence" tests of 35 to 60, four 15 to 30, and two 11 to 12. Among 130 syphilitic sera the readings were below 10 in 105. Of 158 normal sera, the readings were below 10 (and Henry's test negative) in 151, one with a reading of 21 gave a positive Henry test. In kala-azar titres of 100, 150 and higher are reached. The authors conclude that "surfloculence" and melano-flocculation are due to the same principle. Indeed, Chorine (1934) prefers the simpler test with distilled water, measured with the photometer. The melano-flocculation, according to him, is due chiefly to an increase in the euglobulins of the blood helped to some extent by the augmentation of cholesterin and uric acid. The reaction is inhibited by an increase in the molecular concentration of the blood, which accounts for the disappearance of the reaction during the paroxysm. Trensz (1935), however, believes that the two phenomena are different; that "surfloculence" is due to a reaction between the euglobulins and the distilled water, whereas "flocculation" is due to the reaction of the euglobulins and melanin. For, if the melano-flocculation is carried out with melanin in 0.3 per cent ammonium sulfate instead of water, "surfloculence" is suppressed while flocculation with melanin remains. But Chorine (1935) carried out both tests (surflocculation and melano-flocculation) in various concentrations of ammonium sulfate ranging from 1 to 10 per cent. The salt diminishes the flocculation in both series until it is suppressed. The degree of flocculation in the melanin series is higher than in the distilled water series, but the two curves are almost parallel and therefore it is evident to him that melanin acts solely as an indicator. The recent work of Sinton and Ghosh on the chemical nature of hemozoin demonstrates that malarial pigment and melanin are quite different chemical compounds. It would seem that the proponents of the specific-antigen-antibody-reaction theory of the melano-flocculation test are bereft of all trace of evidence in favor of the theory.

Two papers on cutaneous reactions have appeared recently. Moufel and Andreeva - Budylina (1934) tested the "malaren-antigen" of Tsechnowitzer and Moldawskaya-Kritschewskaya intracutaneously on 62 cases of malaria and 72 controls and obtained positive reactions in 72 per cent of the former and 66.6 per cent of the latter. The reaction was thus proven to have no diagnostic value. Trensz (1934) confirmed the observation of Rocchi that intracutaneous injection of hemozoin produced a wheal in non-malarial patients and not in malarial patients. And he obtained similar results with Seichi's melanine and metharfer Bouty.

A note which may be of interest to workers in diagnostic laboratories is that of Hoffman (1935). For staining poorly made blood smears (usually too thick) sent to the laboratory for diagnosis of malaria he fixes only the thinner part and then stains with Giemsa so that the result simulates the ordinary thick-and-thin films. For staining thick films Fróes (1934) recommends an acid solution of methylene blue (1 gram methylene blue, 0.5 c. c. hydrochloric acid, 90 c. c. distilled water, 10 c. c. of 90 per cent ethyl alcohol). The solution is applied to the dry film for 1 to 2 minutes and the slide is then washed in water till the film has a greenish-yellow color. Landeiro applied the technic of determining the rate of sedimentation of red corpuscles preliminary to making thick films and found that blood taken from: (1) the lower part of sediment in the pipette yields preparations eight times richer than the ordinary thick drop; (2) the middle part, six times richer; (3) the upper part, four times richer; and (4) the lower part of the sediment of the mixing tube, six times richer than the ordinary thick drop.

Warnock (1935) studied the differential blood count according to Schilling and observed:

"In 15 cases of typhoid fever, 11 cases of undulant fever and 10 cases of malaria, that beside the low white cell count and frequent lymphocytosis, during the height of the fever there occurred regularly a concurrent marked left shift of polymorphonuclear neutrophilic leukocytes where the young band forms tended to outnumber the mature segmented cells. In the majority of cases where these diseases had been questioned but not proven, this blood picture was absent. In those cases where this blood picture has been present with suggestive clinical symptoms it has been followed by confirmative laboratory findings."

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A REVIEW OF SELECTED PAPERS CONTRIBUTING TO THE PROGRESS OF MALARIA THERAPY DURING THE PAST YEAR*

By BRUCE MAYNE†
Columbia, South Carolina

Kral[1] (1934) contributes a significant picture of the historical aspects of the original induced-malaria treatments. The Berlin charity hospital records based on observations of ten to fifteen years of presumed permanent cures of paresis now reveal that the results of malaria treatment are not highly satisfactory so far as complete and permanent remissions are concerned. In the early treatments, malaria only was given and the alleged cures of 25 to 30 per cent over an observation period of fully fifteen years have dwindled to 20. The author now advocates the giving of malaria treatment followed by a course of arsphenamine-bismuth. Much better results are obtained by preventing late neurosyphilis by abortive treatment of the syphilis. The malaria treatment is preferred to other methods of fever treatment and when contraindications are involved resort is made to mechanical fever treatment.

Yates[2] (1934) records results of treatment of tabes with malaria, of value because cases treated at the same time by the usual chemical agents are shown in parallel. It may be noted here that generally tabes is included among the contraindications for malaria therapy. Among the 32 tabetics treated with malaria 11,

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*Read before National Malaria Committee (Conference on Malaria), meeting conjointly with Southern Medical Association, Twenty-Ninth Annual Meeting, St. Louis, Missouri, November 19-22, 1935.

†Special Expert, U. S. Public Health Service.

or 34 per cent, showed good results. In 8 of these cases no other treatment was offered.

The author concludes that in the degenerative stage tabes is incurable, but in the inflammatory stage, when the cell content and albumin content are high and the degenerative changes are of short duration, malaria treatment may be offered as likely to be effective.

Tobias[3] (1934) successfully reviews the contributions flooding the literature in the past ten years on the effects of various pyrogenic agents in the treatment of general paralysis and tabes dorsalis.

With the passing of sodoku, relapsing fever and sulfur from favor in America, two schools of thought have survived in attempts at further research in pyretotherapy: the malarialists and the physicists. In the author's opinion the great value of malaria therapy lies in the prevention of syphilis of the central nervous system. In resistant types of late and congenital syphilis malaria has also proven its worth. The tissue reaction produced by malaria is much more phagocytic than the monocytic reactions produced by other pyrogenic methods. At the present time the future of electric pyretotherapy cannot be predicted.

The author contributes his own investigations in the clinical results of 175 cases of early neurosyphilis treated with malaria: 81 cases greatly improved, or 46.8 per cent; good reactions in 70 cases, or 9.7 per cent; aggravated or relapsed 4 cases, 2 per cent; extracerebral recidives 2 cases, 1.1 per cent; 1 patient died, 0.5 per cent. The best results were obtained in the taboparetic and asymptomatic groups. No constant relationship was noted between clinical and serological improvement.

Jones, Rathmell and Wagner[4] (1935) report 4 cases in which blood from donors with positive serological findings of syphilis was inadvertently given. In one instance clinical evidence was produced, indicating that syphilis was transmitted by blood transfusion, the patient dying of early neurosyphilis.

This information should be precautionary in connection with the increased application of malaria-infected blood derived from syphilitics. This source of malaria is often the only material available and has induced other types of insanity, gonorrheal arthritis and nonspecific conditions. This occasional accidental conveyance of infection emphasizes the desirability of mosquito-borne malaria.

Solomon and Epstein[5] (1935) discuss a series of 173 patients treated since 1925. During the first six years the results were as follows: 63 patients, 36.4 per cent, were improved and rehabilitated socially; 21, or 12.1 per cent, were improved, but not sufficiently to resume their former occupations; 26, or 15 per cent, were improved, but still hospitalized; in addition 13.8 per cent were unimproved; 22.5 per cent were dead.

The serological results in 75.0 per cent of these patients four to ten years following malaria therapy were regarded as improved. In fact, the analysis showed that in 36.7 per cent the spinal fluid was completely normal and greatly improved; that it was somewhat improved in 39 per cent of the 169 patients examined.

The authors conclude that the process of dementia paralytica can be arrested in a great majority of cases if treatment is instituted, if the general condition warrants it, before the disease has progressed too far.

Normal and nearly normal reactions of the spinal fluid are obtained in the course of years in so large a percentage of cases that life expectancy is increased and the progress of the mental disease is arrested. The authors conclude that a combination of other treatments with malaria gives more satisfactory results than with malaria therapy alone.

Cullins, Morgan and Seymour[6] (1935) give the results of diathermy treatment in 133 patients of a total of 205. Improvement was noted in 90. During the same period 78 other paretics were inoculated with malaria. It is the conclusion of the writers that malaria is the best treatment for this disease and that diathermy is the best substitute when for any reason it is not possible to give the malaria.

It may be noted in an analysis of these diathermy treatments that an equal or greater number, in this instance 15.6 per cent, of unreceptive cases were encountered as is usually found in the administration of malaria.

Schreiner and Wendlberger[7] (1935) treated with malaria 97 cases of gonorrhea and 248 of syphilis. Among all of these cases there were no deaths reported, and only ten had to be discontinued on account of complications.

This treatment is advised for all syphilitics whose reactions have not been reduced to negative by three years' combined treatment with chemical agents, particulary in such patients who have suffered clinical or serological recurrences.

Malaria therapy is also advised for all cases of gonorrhea in women and men who have frequent recurrences. In the latter disease the same contraindications as observed in the treatment of paresis should be stressed.

Paulian[8] (1935) reports that in ten years of malaria therapy in Bucharest 1,070 patients, or 85 per cent, out of 1,224 responded. The treatment (injections) was changed from subcutaneous at first to the intravenous method. He advocates a minimum of twelve distinct paroxysms, depending on the physical condition of the patient.

During ten years of observation the complete clinical remissions numbered 401 persons, more than 37.4 per cent. In addition, 449 showed definite improvement,

156 remained stationary, and the death rate over the ten-year period was less than 6 per cent.

Freeman[9] (1935) concludes that remissions secured with malaria are more complete and lasting than those obtained by any other method.

"When patients have continued at their former level of efficiency for from five to ten years and show only the persistent neurologic signs and no deviation from normal in the body fluids, it is almost permissible to speak of a cure."

The author treats patients in early stages of neurosyphilis in their homes. The patient may even carry on his usual occupation and admission to an institution, with its unavoidable stigma, becomes unnecessary.

Bostroem[10] (1935) presents the medicolegal phases of malaria-treated paresis. He comments that the treatment of paresis with malaria has brought up medicolegal questions that did not exist previous to malaria therapy, when paralytics fell into complete dementia and died within a short time. There are questions of legal responsibility for crimes and misdemeanors, of capacity for assuming responsible positions, of divorce and marriage, and in woman, of the justification of legal abortion in cases of partial or complete recovery under malaria treatment. The decision must be made on the basis of the psychic rather than on the neurologic or serologic findings. In those that have recovered with defect the degree of mental capacity that still persists must be estimated. If the patient is to be considered cured all possible tests must be made to ascertain that there is really no defect left.

The author reminds us that few cured or partially cured paralytics, many of whom were previously criminally insane, commit crimes. Among 2,232 malaria cures reported only 9 patients, 0.4 per cent, have committed criminal acts. It is obvious, he points out, that a patient must be adjudged legally responsible if he is to be given a motor driver's permit or allowed to become a locomotive engineer or ship's captain or follow any other very responsible calling such as physician, judge, teacher, postmaster or bank president. This is even a more difficult decision than the one in regard to criminal liability, because the instituting of malaria treatment for the former has reference only to one past act, while the latter assumes responsibility for the patient's whole future. It is emphasized that cured or remittent paralytics who can carry on their old occupations are often incapable of taking over a new employment, as they have not the adaptability necessary to carry on different work.

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MALARIA MORTALITY IN THE SOUTHERN UNITED STATES FOR 1934 WITH SUPPLEMENTARY DATA FOR PREVIOUS YEARS*

By C. C. Dauer, M.D.
and
Ernest Carroll Faust, Ph.D.
New Orleans, Louisiana

In previous reports[1] on malaria mortality in 14 states of the southeastern United States data were presented and reviewed for the years 1929 to 1933, inclusive. This report will present the mortality data for individual states and counties for the year 1934 in comparison with previous years and will add certain other information relative to malaria mortality in this area.

Reports were received from all the states on the number of deaths from malaria in each county. We acknowledge our indebtedness to each state health department for its splendid cooperation for tabulating and providing these figures.

A large map has been prepared showing the average mortality over a period of five years for each county in the area, with the exception of those located in Texas, where a four-year average was used. It indicates that there are two major and one minor endemic areas so far as mortality is concerned. One of these major areas includes parts of South Carolina, Georgia, Florida and Alabama; and the other is comprised of southeastern Missouri, the extreme western part of Tennessee and Kentucky, the eastern half of Arkansas, the delta counties of Mississippi and northern Louisiana. The minor endemic area includes a few counties in

*Read before National Malaria Committee (Conference on Malaria), meeting conjointly with Southern Medical Association, Twenty Ninth Annual Meeting, St. Louis, Missouri, November 19-22, 1935.

*From the Departments of Preventive Medicine and Tropical Medicine, Tulane University School of Medicine.

southwestern Oklahoma, northeastern Texas, and southwestern Arkansas.

It is extremely interesting that a map published by Maxcy[2] in the Public Health Reports in 1923, showing the average mortality by counties for 1919 to 1921, inclusive, covering this same area, is almost a counterpart of the map we have prepared. Not only are the outlines of the endemic areas approximately the same, but the mortality rates are quite similar except in Virginia and North Carolina.

Higher mortality rates prevailed in the eastern endemic area than in the western for the five-year period from 1929 to 1933. Not only were there more counties in the former with excessively high rates (100 or more per 100,000 population), but the actual rate (38.2) was higher than in the latter group (26.8).

In the graph (*Fig. 1*) which has been shown in previous years, except for the 1934 data the mortality rates by years indicate that the states in the western endemic area have had their peaks a year earlier than the states in the eastern area. Not only in the most recent cyclic wave (1932-1934) was this true, but also in the preceding one (1927-1929). This is shown more clearly in *Fig. 2*. This difference in peak years is quite consistent for each area and probably is significant. However, there does not appear to be any adequate explanation for this variation.

Fig. 2 also shows rather strikingly that there has been little change in mortality rates since 1920 for the five states indicated on the chart. Examination of data from the other states indicates a similar condition except for North Carolina and Virginia. In these two states malaria mortality has declined, but excessively high rates have not been registered there since records have become available. Data previous to 1914 are not available for any state in the endemic area, consequently we can only conjecture that mortality in the decade previous to 1920 was probably generally higher than it now is.

When the data for 1934 are compared with previous mortality figures by counties the following facts are brought to light. Since a grouping of all the counties in each of the major endemic areas gives one a better idea of the true picture, they have been grouped more or less arbitrarily. From the large map showing the average mortality for five years, counties in each major endemic area were listed. The average mortality rates per 100,000 population for the western and eastern areas for the years 1929 to 1933, for 1933 separately, and for 1934 were then calculated and are listed below:

	1929-33	1933	1934
Eastern endemic area	38.2	39.7	50.7
Western endemic area	26.8	50.6	41.2

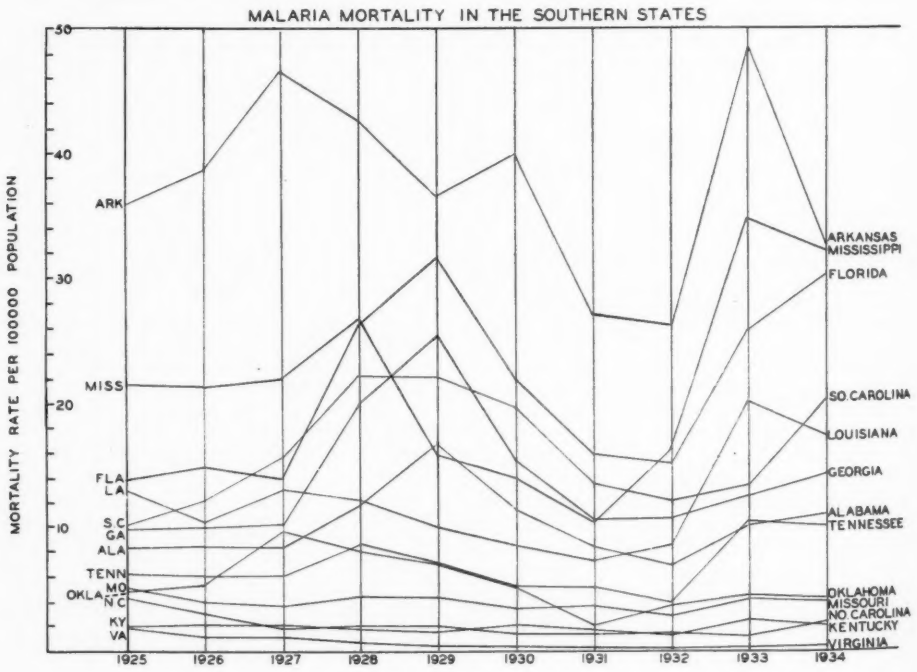

Fig. 1

It is apparent that, although the counties in the western major endemic area had a lower five-year average rate from 1929 to 1933, the rates for each area reached the same height in their peak years, 1933 for the western and 1934 for the eastern.

In the accompanying *Table 1* the data for each state and the various counties are given in more detail. The average malaria mortality rates for 1929 to 1933, 1933 and 1934 are tabulated for each state, for the counties found in endemic areas, and for the remainder of the state. The large map was used in grouping the counties as described above.

In Alabama a few counties in the southeastern section of the State form a part of the large eastern major endemic area. Another group in the southwestern section might be classed as a minor endemic area. The mortality rates are approximately the same for each area, the only difference being the year in which the peak occurred. The remainder of the State furnished the largest proportion of the malaria deaths, but had

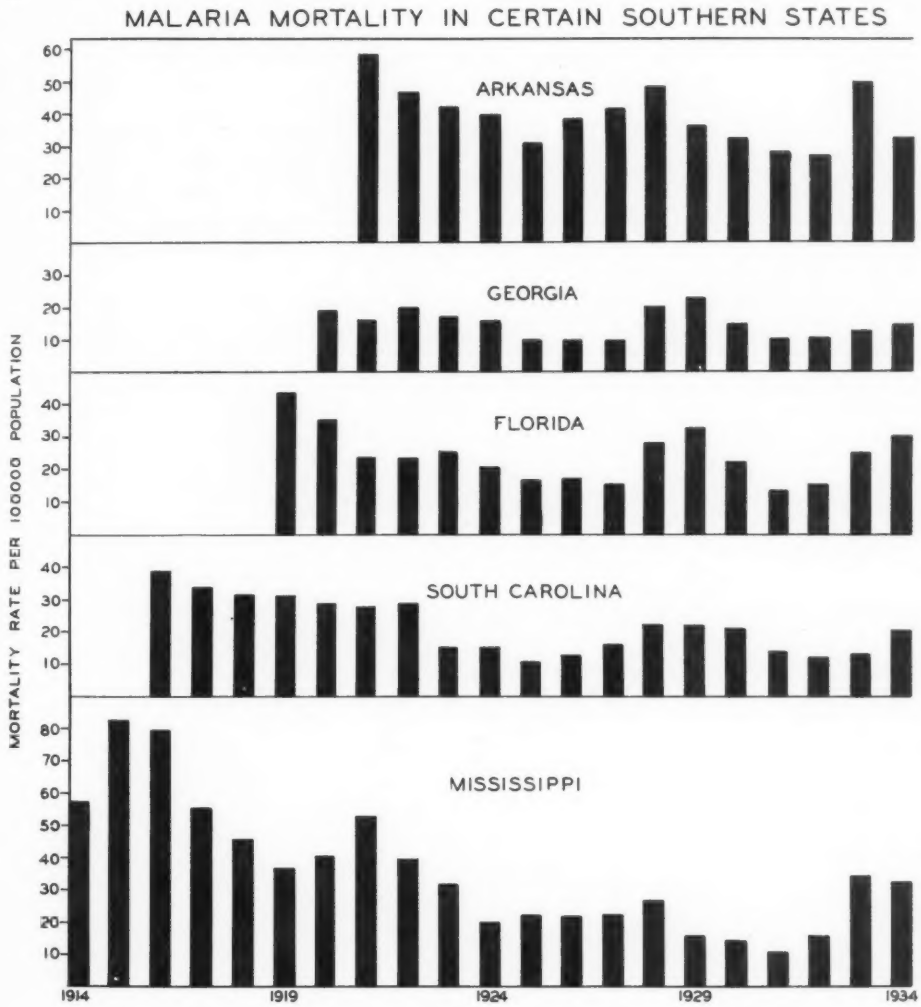

Fig. 2

Table 1

MALARIA MORTALITY RATES PER 100,000 POPULATION
BY STATES AND BY GROUPS OF COUNTIES,
1929-1933, 1933 AND 1934

States and Locations of Endemic Areas	No. of Counties	Population	1929-1933		1933		1934	
			Per Cent Total Malaria Deaths in State	Death Rate per 100,000	Per Cent Total Malaria Deaths in State	Death Rate per 100,000	Per Cent Total Malaria Deaths in State	Death Rate per 100,000
Alabama	68	2,646,248	100	10.5	100	10.2	100	11.1
Southeast	6	187,015	19	26.3	9	13.7	14	25.1
Southwest	8	200,944	18	23.6	17	23.3	10	14.3
Rest of State	54	2,258,289	63	7.2	74	8.7	76	9.8
Arkansas	75	1,854,482	100	34.9	100	48.8	100	32.4
East	21	643,433	52	52.9	55	77.3	60	56.1
Southwest	16	299,869	14	30.7	14	42.0	10	20.0
Rest of State	38	911,180	34	21.4	31	30.9	30	20.0
Florida	67	1,468,211	100	21.9	100	25.4	100	30.3
North central	35	572,239	79	44.7	74	48.4	86	67.1
Rest of State	32	885,972	21	7.6	26	10.7	14	6.8
Georgia	161	2,908,506	100	14.5	100	12.5	100	14.4
Southern	66	1,054,269	83	33.1	83	28.6	86	34.2
Rest of State	95	1,854,237	17	3.8	17	3.3	14	3.1
Kentucky	120	2,614,589	100	2.0	100	2.9	100	2.4
Western	12	189,266	59	16.3	60	23.8	54	18.0
Rest of State	108	2,425,323	41	0.9	40	1.2	46	1.2
Louisiana	63	2,101,593	100	10.6	100	20.2	100	17.5
Northern	29	799,427	70	19.6	77	40.9	77	36.0
Rest of State	34	1,302,066	30	4.9	23	7.6	23	6.3
Mississippi	82	2,009,821	100	17.8	100	34.5	100	32.1
Delta counties	11	418,003	44	37.7	46	75.3	43	66.0
Bluff counties	13	301,519	19	22.7	20	43.1	18	38.8
Rest of State	58	1,290,299	37	10.2	34	19.4	39	19.7
Missouri	114	3,629,367	100	4.0	100	4.4	100	4.2
Southeast	12	269,563	77	42.3	81	60.3	81	56.5
Rest of State	102	3,359,904	23	0.9	19	1.1	19	1.0
North Carolina	100	3,170,276	100	1.6	100	1.2	100	2.5
Coastal region	27	550,195	51	4.7	52	3.8	39	5.4
Rest of State	73	2,620,081	49	0.9	48	0.7	61	1.8
Oklahoma	77	2,396,040	100	4.6	100	4.8	100	4.4
Southeastern	8	219,643	44	22.1	55	28.6	55	27.3
Rest of State	69	2,176,397	56	2.9	45	2.4	45	2.2
South Carolina	46	1,738,765	100	15.9	100	13.2	100	20.5
Coastal region	14	421,586	68	47.8	80	43.9	80	67.3
Rest of State	32	1,317,179	32	5.4	20	3.5	20	5.5
Tennessee	100	2,616,556	100	6.4	100	10.4	100	10.1
Western	26	838,150	87	17.4	91	30.0	80	25.3
Rest of State	74	1,778,406	13	1.3	9	1.3	20	3.0
Texas								
Northwest	17	411,049		19.2		28.7		25.3
Virginia		2,421,851		0.5		0.3		0.4

a relatively low death rate as compared with the endemic areas.

In Arkansas the eastern part of the State (21 counties) furnished over half of the deaths in the five-year period, and more than half in 1933 and 1934. The death rates were excessively high, the highest for any group of counties in the Southern states. The western group of counties, 16 in number, furnished a small percentage of the total deaths for the State, but the death rates were moderately high. The remainder of the State also had comparatively high rates.

About one-half of the counties in Florida situated in the endemic area furnished three-fourths of the deaths in the State. The marked difference in rates for the two areas of the State is quite apparent and needs no further comment.

Slightly more than one-third of the counties in Georgia furnished more than three-fourths of the malaria deaths. The death rates in the endemic area are moderately high, about ten times greater than those for the remainder of the State.

Twelve counties in western Kentucky furnished about 60 per cent of the deaths of the State. The difference in rates for the 12 counties and the remainder of the State is quite marked.

Northern Louisiana furnished approximately three-fourths of the deaths in that State. It is of interest to those who are acquainted with physiographic conditions in the two parts of the State that there should be such wide differences in mortality rates for the two areas.

Eleven counties in Mississippi, the delta counties, furnished about half of the deaths; and 13 of the bluff counties which border on the former approximately one-fifth in the State. The delta group have experienced relatively high rates; the bluff counties' rates have been moderately high. The rest of the State is above average for all states.

In Missouri, malaria mortality rates have been excessively high in a few of the counties in the southeastern part of the State, which contributed three-fourths of the deaths from 1929 to 1933, and four-fifths in 1933 and 1934.

Malaria death rates have been low in North Carolina for a number of years. However, the rates have

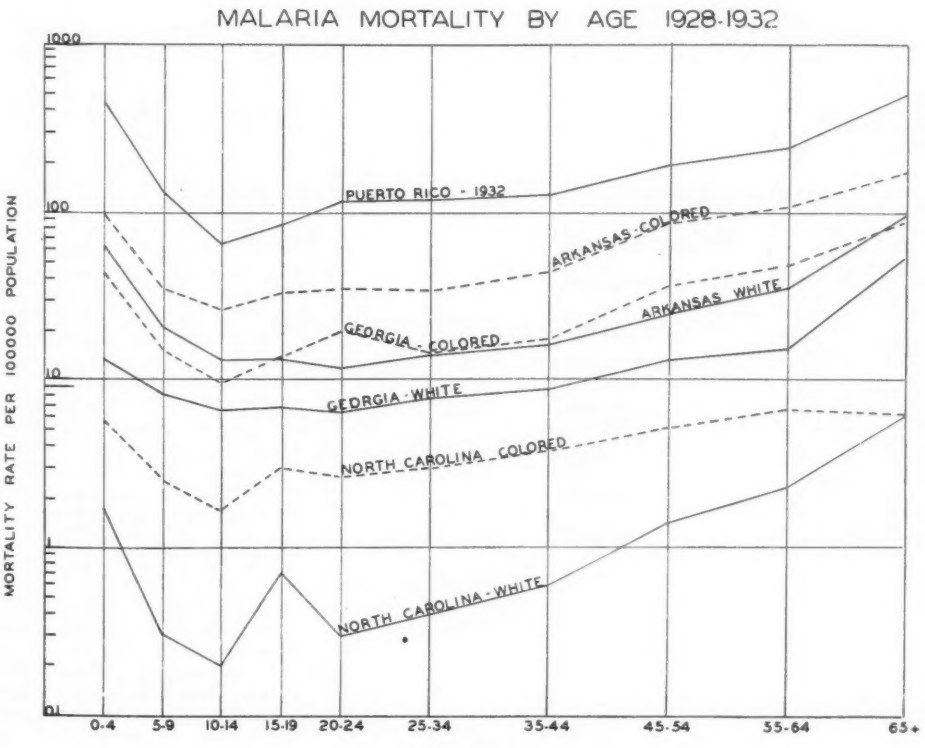

Fig. 3

Table 2

MEAN ANNUAL MALARIA MORTALITY RATES BY AGE FOR WHITE AND COLORED POPULATION 1923-1927 AND 1928-1932

White	0-4		5-9		10-14		15-19		20-24		25-34		35-44		45-54		55-64		65+	
	1923 1927	1928 1932	1923 1927	1928 1932	1923 1927	1928 1932	1923 1927	1928 1932	1923 1927	1928 1932	1923 1927	1928 1932	1923 1927	1928 1932	1923 1927	1928 1932	1923 1927	1928 1932	1923 1927	1928 1932
Alabama		8.4		6.3		4.6		4.5		3.8		4.9		6.6		9.7		10.8		42.2
Arkansas		61.7		20.5		12.8		12.9		11.7		14.5		16.8		24.8		34.5		94.9
Florida	32.8	32.1	14.9	19.6	12.2	9.7	7.9	10.5	9.5	11.9	8.5	10.5	11.5	13.7	14.2	17.5	20.4	23.1	49.0	54.0
Georgia		13.8		8.0		6.4		6.8		6.1		7.6		8.7		12.6		15.3		52.1
Kentucky	3.8	3.3	0.7	0.8	0.6	0.9	0.6	0.7	1.2	0.6	1.3	0.6	1.0	0.9	0.9	1.9	1.9	2.2	8.6	7.1
Louisiana	25.6	18.2	6.5	6.4	5.6	5.2	5.4	3.4	4.5	4.4	5.0	3.4	5.2	4.2	7.4	5.8	12.3	9.8	36.9	29.7
Mississippi	36.2	34.4	12.6	13.1	7.6	7.0	8.2	6.5	7.9	7.6	10.1	6.0	10.5	7.1	10.6	11.0	14.7	16.2	52.3	49.1
Missouri*	12.5	10.6	2.8	3.7	3.3	1.5	3.6	2.7	2.6	2.1	2.5	1.9	2.5	2.5	4.0	2.9	4.2	4.5	10.2	10.8
N. Carolina	5.8	1.8	0.9	0.3	1.2	0.2	1.2	0.7	1.0	0.3	1.9	0.4	2.3	0.6	3.2	1.4	4.3	2.3	11.9	6.0
Oklahoma		10.4		2.4		2.6		3.0		2.1		2.5		3.2		4.1		8.3		25.8
S. Carolina	10.8	12.1	3.4	3.9	1.6	3.7	2.1	3.8	2.9	7.1	1.6	7.1	3.4	8.6	4.8	11.0	4.7	10.3	24.3	31.4
Tennessee	11.8	9.8	2.2	3.0	2.3	2.1	2.1	1.4	3.5	3.1	3.0	3.1	3.4	3.8	5.2	4.1	5.1	5.3	24.1	20.1
Puerto Rico*		435.0		136.5		62.8		82.2		116.0		117.5		133.0		198.0		239.0		492.0
Colored																				
Alabama		22.0		14.4		6.2		11.5		11.5		11.4		13.8		22.4		37.2		72.2
Arkansas		96.4		34.2		26.4		32.4		35.1		33.0		43.7		85.7		108.2		173.4
Florida	72.0	61.4	20.6	18.5	15.1	18.5	23.1	24.4	24.4	22.3	14.7	17.5	28.6	28.6	146.3	56.5	51.0	84.7	143.0	178.0
Georgia		42.3		15.4		9.4		13.1		19.5		14.7		17.8		37.0		48.8		87.0
Louisiana	53.1	23.3	15.1	8.2	8.8	4.7	16.6	11.1	13.6	8.0	10.2	6.8	11.7	7.0	17.3	11.1	23.2	18.3	68.0	40.8
Mississippi	82.0	56.1	26.1	22.7	17.5	12.8	20.5	16.7	23.1	16.7	15.0	12.5	20.3	17.7	32.3	24.5	40.4	34.5	93.7	82.5
N. Carolina	18.2	5.6	5.8	2.6	2.2	1.7	5.5	3.0		2.7	6.8	3.0	5.8	3.7	7.0	5.1	11.5	6.7	21.6	6.1
Oklahoma		19.6		4.0		9.0		6.5	6.4	5.2		7.7		10.0		21.4		28.1		6.0
S. Carolina	59.3	65.0	9.5	22.0	10.8	10.0	10.5	15.8	18.3	23.7	21.0	28.7	24.9	26.3	29.5	43.7	31.0	61.2	91.0	89.0
Tennessee	26.2	20.7	7.0	10.3	8.0	5.4	14.5	5.8	11.6	7.3	8.5	10.5	9.6	8.9	17.8	23.2	23.3	26.9	49.4	

*Total population includes colored.

been consistently higher in the 27 counties along the coastal plain than elsewhere in the State.

In Oklahoma, eight counties in the southeastern corner of the State have furnished over half of the deaths in the State. The rate for the eight counties has been moderately high and for the rest of the State relatively low.

One-third of the counties in South Carolina reported three-fourths of the deaths in this State. The endemic area had high rates and the rest of the State low.

Twenty-six counties in Tennessee (one quarter of the total) had more than three-fourths of the deaths. The death rates in the two areas show marked differences.

Northeastern Texas has comparatively high malaria mortality rates. The average mortality for this group of counties for the years 1929, 1930, 1931 and 1933 (1932 figures are not available) was 19.2. The rate for 1933 was 28.7 and 25.3 for 1934. We have not made any calculations for the remainder of the State because we suspect that the figures are not complete. This was discovered too late to make it possible to have a recheck of data. The inaccuracies, if they do exist, have been incorporated in previous reports, but efforts will be made in future reports to rectify these apparent discrepancies.

Few deaths from malaria have occurred in Virginia in recent years. They have been so scattered in the southeastern part of the State that it makes any grouping of counties seem unnecessary.

Two states, Arkansas and Mississippi, have relatively high rates for all groups of counties, whether they are situated in the so-called endemic areas or not. It probably would be nearer the truth to say that all parts of these two states should be classed as endemic. Possibly we should also place Alabama and Florida in the same category.

Data relative to the age distribution of deaths for any disease are of interest and they are no less so for malaria. No figures have been presented in previous reports on death rates by age groups. The rates tabulated in *Table 2* show the average mortality per 100,000 population for the white and colored population of eleven states and for the total population of Missouri. These data were secured from the Mortality Statistics Re-

ports of the United States Census Bureau for the years 1923 to 1932, inclusive. Not all the states were in the death registration area for the entire period, consequently only the years were included which fell in the two five-year periods 1923 to 1927 and 1928 to 1932, inclusive.

The mean annual rates for 1928 to 1932 are shown graphically on a semilogarithmic scale for several states in *Fig. 3*. The states represented on the graph were chosen because their rates were at different levels and could be shown clearly without the confusion of lines crossing one another. Puerto Rico was included to show that the age curve is probably not different in other localities. Data from other endemic malaria areas in other parts of the world could not be found. It can be seen from *Table 2* and *Fig. 3* that all the states show about the same type of curve for white and colored populations.

The rates by age may be divided into three broad age groups: under 15 years, 15 to 35, and over 35 years. In the first the mortality rates are relatively high under 5 years, but decrease rapidly in the next two five-year groups. From 15 to 35 years the mortality rates remain more or less stationary at a fairly low level as compared to the earlier ages. After 35 years there is a very consistent increase in mortality with each succeeding age period. The highest mortality rates for all age groups are found almost without exception in the oldest population group.

The fact that all the states show essentially the same type of curve of mortality by ages is good statistical evidence that it is a true representation of the age distribution curve of malaria mortality in this country. States with a comparatively small number of deaths without exception show the same type of curve as states with many deaths, which makes the mortality curve seem very significant.

It would be extremely interesting to know what the actual fatality rates are for the different age groups. However, reporting of cases of malaria is so inadequate and reports of cases by age groups so lacking that comparisons of case fatality rates by age groups are absolutely impossible.

The data in this report indicate that there are wide gaps in our knowledge of the epidemiology of malaria in the United States which need to be filled. They raise certain questions which should be answered in

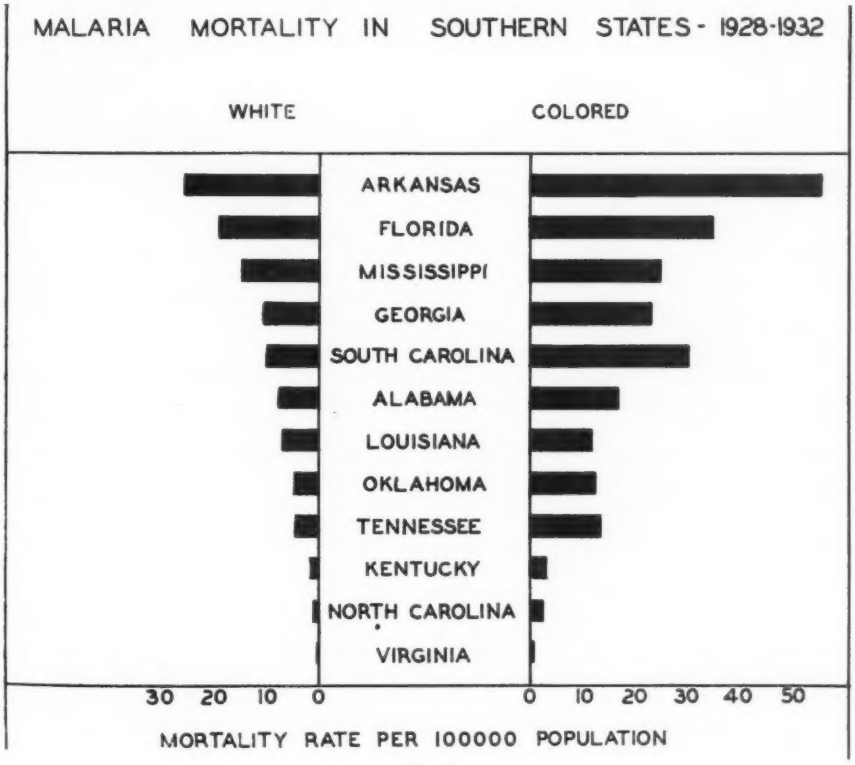

Fig. 4

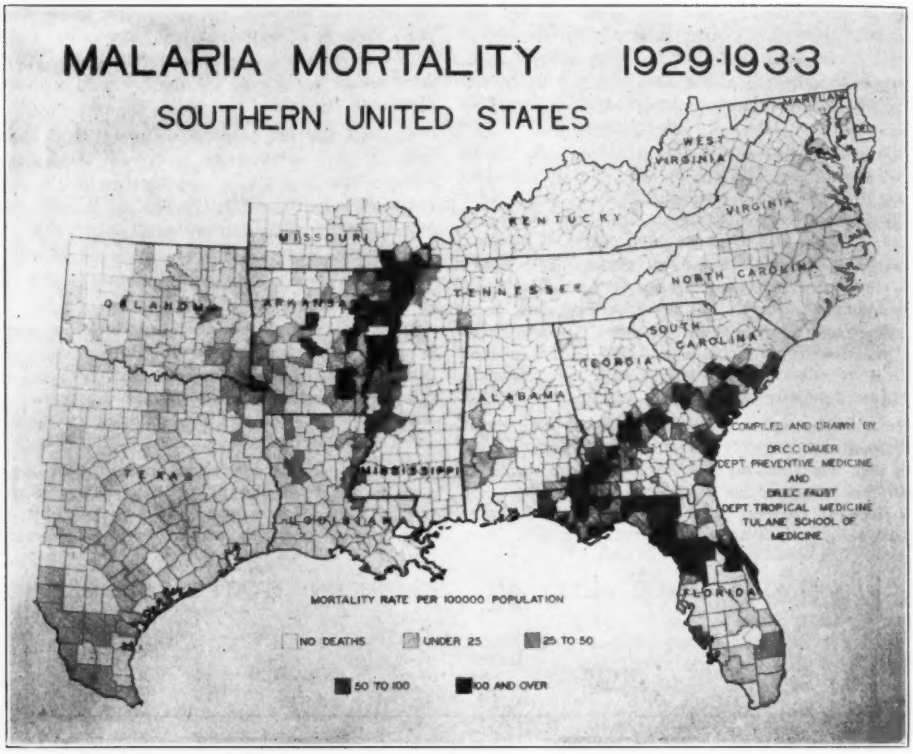

Fig. 5

future studies. Therefore, in the place of a summary we submit the following questions:

(1) It would be of interest to know why there has been no apparent decrease in mortality in the past ten years. We should like to know if the incidence of the disease is also stationary. Case reporting has been too unreliable to warrant answering this question.

(2) What accounts for the differences in the two major endemic areas? Their cyclic peaks are reached in different years. The seasonal peak of cases and deaths also show some differences, but these are less consistent.

(3) Why do the intrinsic cycles occurring every three to four years affect endemic areas as much as other parts of the various states? Does constant contact with malaria fail to protect or are cyclic peaks due to the introduction of new strains of plasmodia? Is it explained by some other cause such as meteorologic changes or conditions favoring increased breeding of Anopheles mosquitoes?

(4) How is the higher mortality of old age to be explained? Are there inaccuracies in the registration of deaths? Do old people die of malaria or are they chronic malaria cases who develop intercurrent infections? Does immunity or tolerance developed in the younger ages last through middle life and then gradually disappear?

Is the ratio of cases to deaths constant throughout life, or higher in certain age groups? If the latter, does this account for the higher mortality of old age?

(5) What type of malaria (tertian, estivo-autumnal, *et cetera*) accounts for the greatest number of deaths? Is the type in any manner related to the age of decedents? In other words, does estivo-autumnal malaria account for a greater percentage of deaths in certain ages than others?

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MALARIA CONTROL ACTIVITIES IN 1935*

By MARK F. BOYD, M.D.†
Tallahassee, Florida

Reports were submitted by the representatives of the state health departments of Alabama, Arkansas, Kentucky, Louisiana, Mississippi, North Carolina, Tennessee and Virginia.

Malaria Incidence.—While the states adjacent to the Mississippi River appear to be experiencing a decline from the peak incidence of 1933 and 1934, the movement of malaria incidence in the states from Alabama eastward has been upward in 1935. A particularly disquieting feature in the states along the south Atlantic seaboard has been the occurrence of small epidemics in the Piedmont and mountain sections in areas heretofore malaria free.

The efforts which have been made in Mississippi for several years past to improve the significance of a malaria diagnosis continue to show productive results. The malaria examinations made in the State Hygienic Laboratory have risen from 5,597 in 1931 to 21,092 in the first ten months of 1935. Mortality reports show that the diagnosis in 33.3 per cent of the deaths attributed to malaria had been confirmed by an antemortem blood examination.

Surveys have been made in a number of states. In Alabama a number of surveys were made about small impounded areas which revealed parasite indices of from 13.5 to 22.7 per cent. The results of the examination of 28,214 of the 53,000 blood smears taken among white and colored school children in 40 Arkansas counties show 2,066 (7.1 per cent) to be positive. The highest incidence observed to date was 19.09 per cent. Examination of 6,410 blood smears taken from 8 of the western counties of Kentucky gives a parasite index of 9.0 per cent for the entire area, the highest incidence observed being 25.3 per cent. Surveys made in different sections of Mississippi revealed indices of from 12 to 35 per cent.

A survey of the anopheline mosquitoes of western Kentucky revealed four species present, namely, *quadrimaculatus, punctipennis, crucians* and *barberi*. From field observations it is thought the first spring brood of *quadrimaculatus* appears about May 10 in the southern part of the State. From 30 to 40 days later the first spring brood appears along the northern boundary. This brood appears to originate from overflow areas.

Malaria Control.—The Federal relief program continued to dominate malaria control. Until August 1 this was sponsored by the FERA and subsequently by the WPA. This program has featured drainage. The accomplishments have been extensive, but the manner in which the figures are given in the various state reports varies so widely that summarization is impossible, although the accomplishments are impressive. In Arkansas and Tennessee various measures for giving permanency to appreciable stretches of their ditches were employed, such as paving, rip-rapping, or sodding.

In some states a considerable amount of screening has been done under this program, thus Arkansas reports 3,000 homes screened.

The impounding program of the Tennessee Valley Authority in Alabama and Tennessee is of great concern to each of these states, the authorities of which are closely observing the malaria control measures of the TVA. On Lake Wilson, Alabama, it was found that larvicidal measures alone could not control anopheline breeding, and that fluctuations in the water level and shore line clearing were also required.

*Summary of reports submitted by state health officers at the annual meeting of the National Malaria Committee (Conference on Malaria), meeting conjointly with Southern Medical Association, St. Louis, Missouri, November 19-22, 1935.

†Secretary, National Malaria Committee.

Southern Medical Journal

JOURNAL OF THE

SOUTHERN MEDICAL ASSOCIATION

Copyright, Southern Medical Association, 1936. Published monthly by the Southern Medical Association, Empire Building, Birmingham, Ala. Annual subscription $4.00. Single copies 35c each.

Entered as second-class matter at the Post Office at Birmingham, Ala., under Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of October 3, 1917, authorized December 20, 1921.

M. Y. DABNEY, M.D., Editor
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Volume 29 JULY 1936 Number 7

EDITORIAL DEPARTMENT

SOUTHERN MEDICAL ASSOCIATION
Thirtieth Annual Meeting
Baltimore, Maryland, November 17-20, 1936

VACCINATION AGAINST TUBERCULOSIS

The history of preventive inoculation against infantile paralysis and against tuberculosis have followed somewhat parallel lines. When Koch discovered the tubercle bacillus he believed that a vaccine and cure were at hand, and since his time an endless number of bacterial products have been offered as specifics for the control of this disease. Similarly, since demonstration that a virus causes poliomyelitis, the virus has been modified for injection in many forms.

The most popular preventive for tuberculosis for a number of years has been the Bacillus Calmette-Guérin, a living attenuated tubercle bacillus grown on special media, pronounced harmless by a great number of investigators, and administered on a large scale abroad to infants and children. It has also been used by a number of American investigators. In Germany four years ago, in the widely publicized Lubeck catastrophe,[1] about a hundred infants inoculated with BCG died within a few months with miliary tuberculosis. All physicians and technicians concerned in the administration and preparation of the vaccine were legally tried for the deaths of the infants. The pathologist who had directed the supposedly prophylactic work declared that he had acted in good faith after careful study, but had erred tragically in judgment, since BCG had suddenly turned virulent. Proponents of the method believed that a preparation of virulent tubercle bacilli had been accidentally exchanged for the original harmless organism. According to Calmette, the vaccine in any case had not been kept on the media which he advocated. The cause of the disaster will never be determined to the satisfaction of all scientists. The trial of course acted as a deterrent to the use of the vaccine in this country. Two years later, in 1933, Dr. William H. Park[2] and his associates in New York City, after extensive injection of children, again reported that BCG was safe for human use, and that it was probably protective against tuberculosis.

Recent development of a new variety of culture medium may throw further light on the subject. The specter of contamination constantly haunts and accuses the bacteriologist, and additional safeguards to sterility are of great moment. Early investigators[3] reported that cultures of BCG may "dissociate," become virulent and produce tuberculosis in guinea-pigs. It was answered that the guinea-pig at times develops spontaneous tuberculosis and that the culture medium of the experiment, that is, the guinea-pig, was tuberculous before it received BCG. Guinea-pig embryo is now being used as a medium for the investigation of infectious disease and may prove better for certain purposes than either the adult or young animal. The fetus may be inoculated intracerebrally with bacteria without terminating pregnancy and is believed to be sterile before the injection unless the mother is grossly diseased. Like the hen's egg, which is now used for the study of virus and other diseases, the fetus offers a living enclosed sterile tissue for the study of bacterial development. In many respects the fetus in the uterus is better protected than the test tube with a stopper.

Neiman and Woolpert,[4] of the University of

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Chicago, have inoculated a large number of guinea-pig fetuses with BCG and have inoculated others with known virulent tubercle bacilli for comparison. Both groups of embryos developed extensive tuberculous lesions of the same character and with equal frequency. The lesions of BCG were slower in appearing, but no difference was detected in the pathologic picture from the virulent and suppposedly avirulent organisms. In the past, only occasional infection of guinea-pigs with BCG has been reported. In the report of the Chicago investigators, constant production of the disease was observed, unless the dosage was very small.

Possibly the guinea-pig fetus, usually protected by the placenta against microbic attack, contains no antibodies of its own and offers an exceptionally fertile field for bacterial growth. This large scale production of tuberculosis with BCG is surprising and confirmation of the work will be required. However, as in the case of the vaccines for prevention of infantile paralysis, one report that the preventive has induced the disease outweighs a hundred that it is harmless.

TIME FOR INSULIN INJECTIONS

Since its discovery, insulin has been popularly administered immediately or within thirty minutes before meals, which makes it urgent that the patient then eat the meal. According to Sindoni,[1] of Philadelphia, hypoglycemia may develop five minutes after insulin is administered, and it may come on thirty minutes after a meal has been taken. The rate of absorption of carbohydrate depends on the cardiovascular system of the diabetic and the duration of his disease. Usually the greater the arteriosclerosis the slower the absorption from the alimentary tract. Sindoni suggests that a steadier blood sugar level with increased comfort of the patient may be secured if insulin is given after instead of before meals.

Rogers,[2] of Lincoln, Nebraska, is also among those who are studying the variability of the blood sugar of patients under insulin therapy. He notes that the sugar level changes even in the same patient under constant insulin dosage. In a group of twenty-four of his patients on a carefully measured diet, about half showed an increase of blood and urine sugar which started soon after midnight and lasted till nearly noon. Sugar was lower in the afternoon and early night. In several patients a change in the timing of the insulin injections was beneficial. In a child of 12 years who had had many insulin reactions and been in insulin coma twice, and also in other patients, he found great improvement if the morning injection was given at 4:00 o'clock instead of just before breakfast. Exercise reduces the blood sugar, and no doubt the long night's rest is an important factor in the morning rise of the diabetic's blood sugar.

These observations are painstaking and valuable. However, all experiments upon insulin timing will become obsolete, or at least will have to be rechecked, when protamine insulin,[3] a new slow acting compound, is put on the market. According to Joslin, its introduction will mark a new era in diabetic therapy. A report of a series of cases treated with protamine insulin by Bowcock,[4] of Atlanta, appears in this issue of the JOURNAL. The new compound would seem to be especially effective in combating the morning rise of blood and urinary sugar which has troubled many clinicians.

GLEANINGS FROM RECENT JOURNALS

Blood Stimulating Principle in Urine.—The reticulocyte, precursor of the red cell, became clinically significant with the discovery of the modern treatment for pernicious anemia. Ordinarily the young human erythrocytes form only about 1 per cent of the total red count. In certain anemias they may be higher. Treatment with fresh liver, liver extracts, and other potent organic material causes a prompt rise in the number of circulating reticulocytes. For several years this rise has been used as an indicator, and drugs now recommended for pernicious anemia are standardized by administration to a patient in the acute stage of the disease, with observation of the effect on the reticulocyte count.

The erythrogenic principle is believed to be

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formed by interaction of food in the stomach with the normal gastric juice, and subsequently to be stored in the liver. The kidneys also contain the potent substance. According to Wakestein and Brunner,[1] of the University of Louisville, it circulates in the blood and should be excreted in part in the urine. They have conducted experiments to test its presence there. If normal pigeons are given liver extracts, the reticulocyte count rises as in human beings. A rise is also stimulated by injection of normal unheated human urine, some urines being more potent than others. The Louisville workers conclude that urine contains an erythrocyte stimulating principle, which may be identical with the anti-anemia principle obtained freely from animal livers.

Urine is the source of potent hormones, as the ovarian, pituitary, and testicular, which sometimes appear in it in great quantities. Excess vitamin C is excreted in the urine. It would not be surprising to find that urine contains regularly also some of the anti-anemic principle.

Tetany Treated with Parathormone.—Aub and his coworkers have described changes in blood and urinary phosphorus and calcium which typify failure of parathyroid function. Pincus and Gittleman[2] report the case of an infant without rickets, but with tetany, whose blood phosphorus was considerably higher than its blood calcium, an abnormal finding characteristic of hypoparathyroidism. Injections of parathormone stopped the convulsions and reversed the calcium-phosphorus ratio to normal. After several periods of treatment the child recovered and developed normally.

Virus Diseases in the Guinea-Pig Fetus.—The virus of vaccinia ordinarily has little effect upon the guinea-pig, though the rabbit is highly susceptible. If the guinea-pig embryo is inoculated and permitted to develop, however, typical lesions are produced in the principal organs, including the skin; they are most common in the lungs and kidneys.[3] Passage through a series of fetuses is reported not to make the virus more virulent for the guinea-pig itself, or for the rabbit.

The guinea-pig fetus is susceptible also to submaxillary gland virus,[1] even if the mother is immune. The young animal is susceptible, but the fetus is better adapted for study of the disease, since spontaneous infections may be eliminated.

1. Wakestein, G. E.; and Brunner, H. D.: Presence in Normal Urine of a Reticulocyte Stimulating Principle for the Pigeon. Arch. Int. Med., **57**:1032 (May) 1936.

2. Pincus, J. B.; and Gittleman, I. F.: Infantile Tetany: A Metabolic Study. Amer. Jour. Dis. Child., **51**:816 (April) 1936.

3. Stritar, J.; and Hudson, N. P.: Susceptibility of the Guinea Pig Fetus to Vaccinia. Amer. Jour. Path., **12**:165 (March) 1936.

TWENTY-FIVE YEARS AGO

From Journals of 1911

Silver Nitrate Irrigations in Diarrhea of Infants.[2]—"Various astringents have been advocated for the local treatment of the intestine of infants ill with infectious diarrhea. * * * During the last season at the Boston Floating Hospital colon irrigations of 3 per cent silver nitrate were employed. * * * Since no harm has been done * * * and some good results have been obtained, it would seem worth while to give this means of treatment further trial."

Sand for Infected Wounds.[3]—"Thiers * * * has employed in severely infected wounds with much satisfaction a method of treatment which is based upon the ability of fine sand to exert capillary attraction upon fluids. * * * The suppurating wound or sinus is covered with sand until the involved portion of the body, as the forearm, lies in the sand bath. * * * The secretion is quickly drawn from the wound so that the sand in the immediate neighborhood of the wound should be changed frequently. This the patient can manage with a spoon.

"* * * The edema and inflammation quickly disappear, the granulations become full and bright red and the cicatrization progresses favorably. * * * The method is also suited to the after treatment of skin grafting."

Resection for Malignancy.[4]—"Dr. Thomas S. Cullen * * * reported the case of a patient in whom a malignant growth was suspected. * * * The uterus was amputated through the cervix and with the tubes and ovaries turned up on the surface of the tumor. The appendix was next amputated * * * about three feet of bowel were then clamped off and the mesentery of the small bowel containing the tumor gradually tied off. All the structures mentioned were removed in one piece, as it would have been absolutely impossible to separate the uterus without entering the cancerous mass and opening up the bowel."

1. Markham, F. S.; and Hudson, N. P.: Ibid, p. 175.

2. Smith, Richard M.: Silver Nitrate Irrigations in the Treatment of Infectious Diarrhea in Infants. Boston Med. & Surg. Jour., **164**:298, 1911.

3. Abst. Amer. Jour. Med. Sci., **142**:136, 1911.

4. Report of Sou. Surg. & Gyn. Assn. Boston Med. & Surg. Jour., **164**:310, 1911.

Baltimore—Where We Meet

Southern Medical Association, Thirtieth Annual Meeting, Baltimore, Maryland, November 17-20, 1936

BALTIMORE*

A city of active industry and commerce, busy factories, piers, railroad stations, office buildings, shops and markets, which occupy several hundred thousand workers—this in brief is Baltimore.

Eighth in population in the country (840,000), in the forefront industrially, with close to 2,000 manufacturing plants; fourth port in foreign trade, annually clearing in normal times upwards of 5,000 vessels bringing in and taking away cargoes totaling more than 15,000,000 tons; a city in which 62 per cent of the dwellings are owned by the occupant; a city with a climate officially termed by the United States Weather Bureau as "ideal for permanent residence;" a city rich in American history; the only metropolitan city in America in which is blended the hustle and go of the North and the exquisite culture and charm of the Southland; a center of education, art, science and medical research; a city which is at once the gateway to the South and the Middle West and for the latter section a gateway to the sea as well, such is Baltimore.

Situated in Baltimore are Fort McHenry, the city's chief point of interest; the Johns Hopkins University, Hospital and Medical School, all internationally known; the University of Maryland, including the University's medical school and the Baltimore Dental College, oldest institution of its kind in the world, and closely attached to the University is the University Hospital, recently rebuilt and enlarged; Goucher College for Women; the Peabody Conservatory of Music and Peabody Library; the Enoch Pratt Free Library with 30 branches; the Walters Art Gallery, now municipally owned, which contains one of the finest collections of art in the world; the Maryland Institute of Art and Design, which was the first institution of learning in the United States to establish an airplane engineering course; Loyola College, Notre Dame Academy and St. Mary's Seminary (all Roman Catholic); Morgan College (Negro); the Baltimore Museum of Art (municipally owned) and a public school system as well as private and parochial schools which are among the country's outstanding institutions.

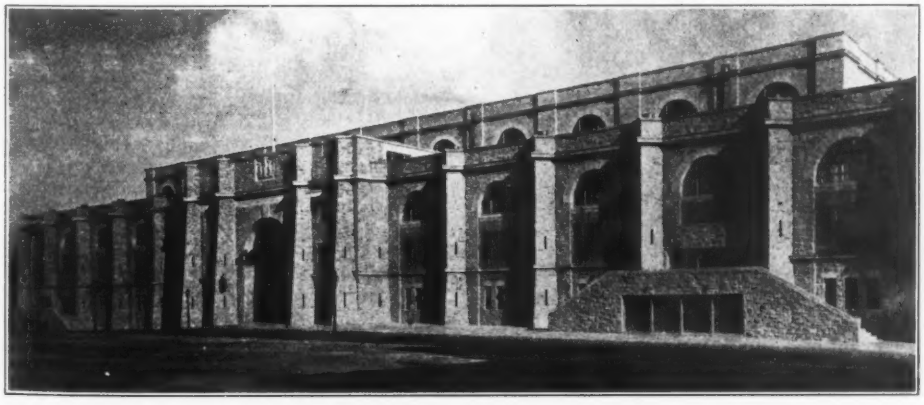
Baltimore long has been known as a convention city because of its rich historical background; its diversified industrial and world-wide commercial activity; its cultural and educational attainments; its proximity to the Nation's capital, to ancient Annapolis, the home of the United States Naval Academy, to Gettysburg, Antietam and other battlefields; its proximity to the Chesapeake Bay, called by the Indians the "Mother of Waters" and by others the "Little Mediterranean of America."

All of these offer almost unlimited post-convention opportunities for recreation or diversion, sight-seeing, fishing, water and land sports.

Baltimore's new convention and exposition auditoriums in the reconstructed Fifth Regiment Armory were designed specifically to accommodate all kinds of conventions and exhibitions. It has 120,000 square feet of floor space in addition to numerous meeting rooms of various sizes, and will seat 10,000 persons. It is within walking distance of all the city's railroad stations and within but a few minutes' ride from any of the hotels.

The city's thirty-three hotels provide ample housing and meeting accommodations, at reasonable rates, for a gathering of practically any size. The larger hotels

*From the Convention Bureau, Baltimore Association of Commerce, Mr. A. Russell Phillips, Director.



FIFTH REGIMENT ARMORY

Here will be held all General Sessions, all Section Meetings, and Scientific and Technical Exhibits—everything under one roof.

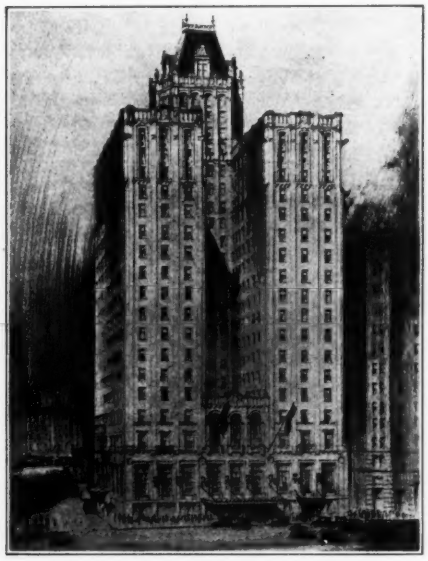
are centrally located and are grouped within a few blocks of each other. They include:

LORD BALTIMORE, Hanover and Baltimore Streets
SOUTHERN, Light and Redwood Streets
EMERSON, Baltimore and Calvert Streets
RENNERT, Saratoga and Liberty Streets
BELVEDERE, Charles and Chase Streets
CONGRESS, Franklin Street, near Eutaw
NEW HOWARD, Howard Street, near Baltimore
STAFFORD, Charles and Madison Streets
ABBEY, 723 St. Paul Street
ALTAMONT, Eutaw and Lanvale Streets
MT. ROYAL, Calvert and Mt. Royal Avenue
ARUNDEL, Charles and Mt. Royal Avenue
BILTMORE, Fayette and Paca Streets

The trained personnel of the hotels understands convention problems and is qualified by experience to render competent assistance and cooperation to all convention organizations regardless of size.

Baltimore also has numerous restaurants where one may enjoy Maryland's famous seafood or other dinners. Oliver Wendell Holmes, in the "Autocrat of the Breakfast Table," termed Baltimore, because of its oysters, crabs, terrapin, fish and wild duck, "the gastronomic center of America."

Because of its geographical situation Baltimore is within overnight reach of 63,000,000 people, or one-half the country's population. The city is easily accessible by land, water or air, is served by three trunk line railroads, three National highways, transcontinental and intercoastal steamship lines and frequent air line schedules connecting with the numerous inter-continental air services. It is the home of one of the largest aircraft manufacturing plants (Glenn L. Martin Company) in America.



LORD BALTIMORE HOTEL
General Hotel Headquarters.

Baltimore is not a one-industry city and has never enjoyed a so-called boom or mushroom growth. Its rise has been gradual through the years. Because of this diversity of industry Baltimore suffers less than other large centers in times of industrial stress in the Nation, and it has ever been so. Some of Baltimore's major industries stand out, however. Among them are included the following:

Baltimore Copper Smelting and Refining Company, the largest in the world.

Bethlehem Steel Company (located within Baltimore's industrial area), the largest plant of its kind in the United States located on tidewater.

McCormick & Company, largest plant in America, and perhaps the world, for the manufacture of spices, extracts, teas, insecticides, etc.

American Sugar Refining Company plant, largest on the Atlantic coast.

Davison Chemical Company, largest producers of sulphuric acid.

Men's clothing and meat packing industries, the annual production of which goes up into millions of dollars.

Other large industries include tin cans and other containers, fertilizers and materials, bottle stoppers and machinery, drugs, medicines, pharmaceuticals, porcelain and enamel ware, cannery products, women's wear, straw hats, paints and enamels, beverages, printing and lithographing, umbrellas and parasols, glass bottles and jars, canning house machinery, work clothes, wire cable, industrial alcohol, electrical apparatus, ice cream, milk products and candies.

Growth of the Port of Baltimore, at first gradual but slow, became more rapid at the close of the World War, due to the activities of the Export and Import Board of Trade, which is now a bureau of the Association of Commerce. Today the port has 30-odd regular overseas steamship services operating on schedule sailing dates to more than 100 world ports. The port is used by 33 states and Canada for routing imports and by 38 states and Canada for routing exports. In addition there are nine services operating in intercoastal trade and ten others in coastwise and Chesapeake Bay services. Baltimore is the third port on the Atlantic Coast in foreign trade and fourth in the United States.

Baltimore is 207 years old. Founded on 60 acres costing $600, it now covers approximately 93 square miles and its assessible basis for taxation is nearly $2,000,000,000. The first tax rate levied (1830) was $4.36½ on the $100. Today it is $2.49. On its two hundredth anniversay it was rechristened the "Old City with a Young Stride."

Book Reviews

Allergy of the Nose and Paranasal Sinuses. A Monograph on the Subject of Allergy as Related to Otolaryngology. By French K. Hansel, M.D., M.S., Assistant Professor of Clinical Otolaryngology, Washington University School of Medicine. St. Louis: The C. V. Mosby Company, publishers. 820 pages with 58 illustrations. 1936. Cloth, $10.00.

Hansel's book is not an introduction to allergy, a primer for students and practitioners. It is rather a source book intended for use by rhinologist and allergist. It is an extremely impersonal volume, reflecting to a negligible degree the experience and opinions of the author. It is scholarly, condensing as it does over twenty-four hundred articles dealing with the subject of allergy and the nasal passages. It is an essential volume for those doing research in allergy or for the serious student of the subject. If one wants merely an introduction to the subject, he must look elsewhere for it.

Basal Metabolism in Health and Disease. By Eugene F. DuBois, M.D., Medical Director, Russell Sage Institute of Pathology; Professor of Medicine, Cornell University Medical College, New York; Physician-in-Chief to the New York Hospital. Third Edition. 494 pages, illustrated. Philadelphia: Lea & Febiger, 1936. Cloth, $5.00.

This book is unique in that it presents in readable style and understandable form the most important problems of metabolism in health and disease. Whether the reader be internist, surgeon, physiologist, dietitian, technician or medical student, there is a store of information of practical importance to him.

It is an outstanding contribution to the science of nutrition, and gives to its reader a more accurate conception of the evaluation of metabolic studies.

Surgical Emergencies in Children. By Harold Clifford Edwards, M.S., London, F.R.C.S., England, Surgeon and Lecturer in Surgery to King's College Hospital, London. 274 pages, illustrated. Baltimore: William Wood & Co., 1936. Cloth, $4.50.

In this volume the author has reviewed under the head of "surgical emergencies," practically all the surgical conditions which appear in a pediatric clinic.

Many of these cannot be classed as emergencies in the commonly accepted meaning of the word, hence the title of the book seems rather misleading.

The author's views on various surgical problems are sound and his advice may, as a rule, be safely followed.

As a guide to the management of surgical diseases and accidents in children the work is acceptable.

The Specificity of Serological Reactions. Karl Landsteiner, M.D., the Rockefeller Institute for Medical Research, New York. 178 pages. Springfield, Illinois: Charles C. Thomas, 1936. Cloth, $4.00.

The phenomenon of serological specificity is presented by this excellent review and discussion, based on the classical experiments of the author and his colleagues.

The author takes up first the specificity of natural antigens and antibodies, then artificial conjugated antigens and the serological reactions of simple chemical compounds, and finally the more recent work on the chemistry of cell substances, carbohydrates and lipoids.

Some of the topics of general interest are: the differentiation and identification of human blood groups, animal species, and bacterial types.

A comprehensive bibliography of over a thousand references is included.

For readers unacquainted with the concepts of serology, explanations are provided.

Modern Operative Surgery. Edited by G. Grey Turner, M.S., F.R.C.S. (Eng.), F.A.C.S. (Hon.), Senior Hon. Surgeon, Royal Infirmary, Newcastle-upon-Tyne; Professor of Surgery in the University of Durham. Volume I, 868 pages, illustrated. Volume II, 896 pages, illustrated. Baltimore: William Wood & Co., 1934. Cloth (2 volumes), $16.00.

The death of H. W. Carson left the arrangements for the second edition of this work in active preparation and the responsibility for its satisfactory completion fell upon Mr. G. Grey Turner. He has been conspicuously successful in turning out a splendid work on operative surgery.

Each chapter has been written by an outstanding English surgeon, and, as is necessary in works on operative technic, each step in the operation under discussion is explained with the utmost detail, and operations are further clarified by numerous illustrations.

Ten chapters on abdominal surgery were from the pen of the late Dr. Carson and have been carefully revised by Turner. Especially interesting is the chapter dealing with surgery of the biliary system.

The chapter on thoracic surgery is by Mr. J. E. H. Roberts, that on plastic surgery is by Sir Harold Gillies, and that on genito-urinary surgery is by Sir John Thompson-Walker; all of whom are well known to the profession in America. Chapters on other specialties are by authors of like distinction.

Textbooks of a few years ago contained little on neurosurgery, less on surgery of the sympathetic system, and nothing on x-ray and radium therapy. In the present work, due attention is given to progress in these fields.

A Text-book of Surgery for Students and Physicians. By W. Wayne Babcock, A.M., M.D., LL.D., F.A.C.S., Professor of Surgery and of Clinical Surgery in the Temple University. Second Edition, Rewritten. 1312 pages with illustrations. Philadelphia: W. B. Saunders Company, 1935. Cloth, $10.00.

This comprehensive one-volume work on surgery is an admirable textbook for students and a ready reference handbook for practitioners.

It is divided into four parts: "General Surgery," "The Surgery of the Systems," "Surgical Technic" and "Regional Surgery."

The first part takes up general surgical pathology and those great constitutional problems, such as hemorrhage and hemostasis, thrombosis and embolism, shock, coma and delirium. Under the heading of "Wounds" is included a section on "Injuries and Dis-

Continued on page 773

OFFICERS 1935-1936

The following is a complete roster of the officers of the Southern Medical Association for 1935-36, and of associations meeting conjointly with the Southern Medical Association:

President—Dr. Fred M. Hodges, Richmond, Virginia.

First Vice-President—Dr. Quitman U. Newell, St. Louis, Missouri.

Second Vice-President—Dr. J. E. Knighton, Shreveport, Louisiana.

Secretary-Manager (Secretary, Treasurer and General Manager)—Mr. C. P. Loranz, Birmingham, Alabama.

Editor of Journal—Dr. M. Y. Dabney, Birmingham, Alabama.

Associate Editor of Journal—Mrs. Eugenia B. Dabney, Birmingham, Alabama.

Councilors—Dr. M. Pinson Neal, Chairman, Columbia, Missouri; Dr. M. Toulmin Gaines, Mobile, Alabama; Dr. Harvey S. Thatcher, Little Rock, Arkansas; Dr. Wm. Thornwall Davis, Washington, D. C.; Dr. Luther W. Holloway, Jacksonville, Florida; Dr. Edgar G. Ballenger, Atlanta, Georgia; Dr. C. W. Dowden, Louisville, Kentucky; Dr. Arthur A. Herold, Shreveport, Louisiana; Dr. Edward A. Looper, Baltimore, Maryland; Dr. Harvey F. Garrison, Jackson, Mississippi; Dr. Paul H. Ringer, Asheville, North Carolina; Dr. W. K. West, Oklahoma City, Oklahoma; Dr. Kenneth M. Lynch, Charleston, South Carolina; Dr. Eugene Rosamond, Memphis, Tennessee; Dr. Guy F. Witt, Dallas, Texas; Dr. Vincent W. Archer, University, Virginia; Dr. James R. Bloss, Huntington, West Virginia.

Board of Trustees (All are Past-Presidents)—Dr. Hugh S. Cumming, Chairman, Washington, D. C.; Dr. Felix J. Underwood, Jackson, Mississippi; Dr. Lewis J. Moorman, Oklahoma City, Oklahoma; Dr. Irvin Abell, Louisville, Kentucky; Dr. Hugh Leslie Moore, Dallas, Texas; Dr. H. Marshall Taylor, Jacksonville, Florida.

Section on Medicine—Dr. William B. Porter, Chairman, Richmond, Virginia; Dr. O. P. J. Falk, Vice-Chairman, St. Louis, Missouri; Dr. John B. Youmans, Secretary, Nashville, Tennessee.

Section on Pediatrics—Dr. M. Hines Roberts, Chairman, Atlanta, Georgia; Dr. T. C. Hempelmann, Vice-Chairman, St. Louis, Missouri; Dr. Hughes Kennedy, Jr., Secretary, Birmingham, Alabama.

Section on Gastroenterology—Dr. James Alto Ward, Chairman, Birmingham, Alabama; Dr. Lay Martin, Vice-Chairman, Baltimore, Maryland; Dr. H. E. Murry, Secretary, Texarkana, Arkansas.

Section on Pathology—Dr. George T. Caldwell, Chairman, Dallas, Texas; Dr. Wiley D. Forbus, Vice-Chairman, Durham, North Carolina; Dr. Roy R. Kracke, Secretary, Emory University, Georgia.

Section on Neurology and Psychiatry—Dr. Frank H. Redwood, Chairman, Norfolk, Virginia; Dr. Lawrence F. Woolley, Vice-Chairman, Towson, Maryland; Dr. Frank H. Luton, Secretary, Nashville, Tennessee.

Section on Radiology—Dr. Henry J. Walton, Chairman, Baltimore, Maryland; Dr. James A. Meadows, Vice-Chairman, Birmingham, Alabama; Dr. Roy G. Giles, Secretary, Temple, Texas.

Section on Dermatology and Syphilology—Dr. Jack W. Jones, Chairman, Atlanta, Georgia; Dr. Harry M. Robinson, Vice-Chairman, Baltimore, Maryland; Dr. Winston U. Rutledge, Secretary, Louisville, Kentucky.

Section on Surgery—Dr. Isaac A. Bigger, Chairman, Richmond, Virginia; Dr. James Barrett Brown, Vice-Chairman, St. Louis, Missouri; Dr. Alton Ochsner, Secretary, New Orleans, Louisiana.

Section on Bone and Joint Surgery—Dr. Robert W. Johnson, Jr., Chairman, Baltimore, Maryland; Dr. Guy A. Caldwell, Vice-Chairman, Shreveport, Louisiana; Dr. Alfred R. Shands, Jr., Secretary, Durham, North Carolina.

Section on Gynecology—Dr. Lee F. Turlington, Chairman, Birmingham, Alabama; Dr. John C. Burch, Vice-Chairman, Nashville, Tennessee; Dr. R. A. Ross, Secretary, Durham, North Carolina.

Section on Obstetrics—Dr. James R. Bloss, Chairman, Huntington, West Virginia; Dr. Warren E. Massey, Vice-Chairman, Dallas, Texas; Dr. Milton Smith Lewis, Secretary, Nashville, Tennessee.

Section on Urology—Dr. Thomas D. Moore, Chairman, Memphis, Tennessee; Dr. Grayson Carroll, Vice-Chairman, St. Louis, Missouri; Dr. Jefferson C. Pennington, Secretary, Nashville, Tennessee.

Section on Railway Surgery—Dr. Ross A. Woolsey, Chairman, St. Louis, Missouri; Dr. J. W. Palmer, Vice-Chairman, Ailey, Georgia; Dr. George A. Traylor, Secretary, Augusta, Georgia.

Section on Ophthalmology and Otolaryngology—Dr. Millard F. Arbuckle, Chairman, St. Louis, Missouri; Dr. Grady E. Clay, Vice-Chairman, Atlanta, Georgia; Dr. Oscar M. Marchman, Secretary, Dallas, Texas.

Section on Medical Education—Dr. Harry C. Schmeisser, Chairman, Memphis, Tennessee; Dr. Russell H. Oppenheimer, Vice-Chairman, Atlanta, Georgia; Dr. Harvey S. Thatcher, Secretary, Little Rock, Arkansas.

Section on Public Health—Dr. Douglas L. Cannon, Chairman, Montgomery, Alabama; Dr. William H. F. Warthen, Vice-Chairman, Baltimore, Maryland; Dr. W. C. Williams, Secretary, Nashville, Tennessee.

American Public Health Association, Southern Branch (meeting conjointly with Southern Medical Association)—Dr. I. C. Riggin, President, Richmond, Virginia; Dr. C. J. Vaughn, First Vice-President, Lexington, Mississippi; Miss Frances Montgomery, Second Vice-President, Montgomery, Alabama; Mr. M. C. Baer, Third Vice-President, Little Rock, Arkansas; Dr. G. F. McGinnes, Secretary-Treasurer, Richmond, Virginia.

National Malaria Committee (meeting conjointly with Southern Medical Association)—Dr. L. O. Howard, Honorary Chairman, Washington, D. C.; Dr. Herbert C. Clark, Chairman, Panama, Republic of Panama; Dr. W. V. King, Chairman-Elect, Orlando, Florida; Dr. George E. Riley, Vice-Chairman, Jackson, Mississippi; Dr. Mark F. Boyd, Secretary-Treasurer, Tallahassee, Florida.

American Society of Tropical Medicine (meeting conjointly with Southern Medical Association)—Dr. Henry E. Meleney, President, Nashville, Tennessee; Dr. Herbert C. Clark, President-Elect, Panama, Republic of Panama; Dr. Alfred C. Reed, Vice-President, San Francisco, California; Dr. N. Paul Hudson, Secretary-Treasurer, Columbus, Ohio; Dr. Charles F. Craig, Editor, New Orleans, Louisiana.

Allergy Clinic and Round Table (meeting conjointly with Southern Medical Association)—Dr. Hal M. Davison, Chairman, Atlanta, Georgia; Dr. Alan G. Cazort, Vice-Chairman, Little Rock, Arkansas; Dr. Charles H. Eyermann, Secretary, St. Louis, Missouri.

Society for Experimental Biology and Medicine, Southern Section (meeting conjointly with Southern Medical Association)—Dr. Harold Cummings, Chairman, New Orleans, Louisiana; Dr. Roy H. Turner, Vice-Chairman, New Orleans, Louisiana; Dr. Alton Ochsner, Secretary, New Orleans, Louisiana.

Southern Association of Anesthetists (meeting conjointly with Southern Medical Association)—Dr. Joseph McNearney, President, Maplewood, Missouri; Dr. Eldon B. Tucker, President-Elect, Morgantown, West Virginia; Dr. Joseph P. Bogan, Vice-President, Washington, D. C.; Dr. Wm. Hamilton Long, Secretary-Treasurer, Louisville, Kentucky.

American Academy of Pediatrics, Region 2 (meeting conjointly with Southern Medical Association)—Dr. Edward Clay Mitchell, Chairman, Memphis, Tennessee.

Women Physicians of the Southern Medical Association—Dr. Pauline Williams, Richmond, Virginia.

Woman's Auxiliary to the Southern Medical Association—Mrs. Oliver W. Hill, President, Knoxville, Tennessee; Mrs. Frank N. Haggard, President-Elect, San Antonio, Texas; Mrs. S. N. Prunty, First Vice-President, Parkersburg, West Virginia; Mrs. Joseph M. Trigg, Second Vice-President, St. Louis, Missouri; Mrs. C. B. Erickson, Recording Secretary, Shreveport, Louisiana; Mrs. W. A. Shelton, Corresponding Secretary, Knoxville, Tennessee; Mrs. E. W. Veal, Treasurer, South Jacksonville, Florida; Mrs. Harvey F. Garrison, Historian, Jackson, Mississippi; Mrs. E. V. Caldwell, Parliamentarian, Huntsville, Alabama.

Continued from page 771

eases Received from Lower Animals," which covers much more ground than is usually found in one-volume works on surgery.

In the second part, the chapters on the blood vessels and lymphatics, the peripheral nerves and the sympathetic nervous system and the ductless glands, are extremely valuable. In these chapters, the author has the opportunity of discussing subjects with which, from his wide clinical experience, he is thoroughly familiar.

In the chapter dealing with fractures some of the newer and more popular methods of treatment are not fully discussed. The most striking omission is that of the convex Bradford frame, the Rogers hyperextension frame, or the improvements of these frames, for the treatment of compression fractures of the vertebrae.

The chapter on "Surgical Therapeutics" covers a wide range, embracing subjects from artificial respiration to the use of radium. The information contained in the chapter on "Intravenous and Subcutaneous Medication" is specially valuable, now that these methods have supplanted oral medication to a great extent.

The chapters on anesthesia and on pre- and post-operative treatment again give the author the opportunity to express himself authoritatively from his wide clinical experience.

The twenty-seven chapters on regional surgery contain in considerable detail the latest methods of surgical treatment of the different regions of the body. Of unusual interest are those sections devoted to the central nervous system, the breast, to thoracic surgery and to surgery of the liver, pancreas, and spleen.

The chapter on hernia is a classic. In addition to covering the subject completely, it is unusually well illustrated. The author describes his own operation for inguinal hernia in which the cord is not transplanted. Very properly, no reference is made to the injection treatment of hernia which has recently been revived in some sections of the country, but which is not meeting with authoritative approval.

Southern Medical News

ALABAMA

Dr. Lloyd Noland, Fairfield, was elected President of the Alabama State Medical Association at its meeting in Montgomery April 20-22.

Dr. Thurston D. Rivers was recently made Medical Director of the Montgomery Tuberculosis Sanatorium to succeed Dr. Beverly Woodfin Cobbs, resigned.

The Gulf Coast Clinical Society has named Dr. William R. Meeker, Mobile, Chairman, and Dr. Mozart A. Lischkoff, Pensacola, Florida, Secretary-Treasurer. The Society was recently organized by physicians from Mobile, Pensacola, Gulfport and Biloxi.

Deaths

Dr. Lawrence Joshua Davis, Dixons Mills, aged 62, died February 11 of disease of the prostate gland.

Dr. Daniel Richard Cornelius, Florence, aged 54, died March 13 of cerebral hemorrhage.

ARKANSAS

The Ouachita County Medical Society had as guest speaker at a recent meeting Dr. Herbert A. Durham, Shreveport, Louisiana.

The Union County Medical Society had as guest speaker recently Dr. Willis C. Campbell, Memphis, Tennessee.

Dr. C. A. Lumsden, DeWitt, has been made President of the Rotary Club of that city.

Dr. Ralph M. Sloan was recently made President of the Jonesboro Rotary Club.

Dr. F. J. Sculy, Hot Springs National Park, has been made a Fellow in the American College of Physicians.

Dr. J. R. Lynn, Hazen, has been made Health Officer of that city.

Dr. J. S. Rhinehart has been made Chief of Staff of the Camden Hospital.

Dr. J. B. Hesterly has been made Vice-President and Dr. A. S. Buchanan Director of the Prescott Rotary Club.

Dr. Wells F. Smith, Little Rock, has been made President of the State Board of Health.

Dr. John C. Pate, Leslie, has been made Mayor of that city.

Dr. N. I. Stebbins has been made Vice-President of the Rotary Club of Nashville.

Dr. A. C. Shipp, Little Rock, has been elected Vice-President of the Arkansas Tuberculosis Association.

Dr. M. J. Kilbury, Little Rock, has been made Sergeant-at-Arms and Dr. S. C. Fulmer, Little Rock, Director of the Little Rock Rotary Club.

Dr. Fount Richardson, Fayetteville, has been made Captain and Dr. N. C. Hodge, Marianna, First Lieutenant of the Medical Corps, Arkansas National Guard.

Dr. L. O. Greene, Pea Ridge, and Miss Emma Howard were married recently.

Deaths

Dr. Thomas J. Woods, Evening Shade, aged 85, died February 18.

Dr. George Aubry Henry, Horatio, aged 69, died February 19.

Dr. R. C. Arbaugh, Booneville, aged 64, died recently.

Dr. Josiah S. Chastain, Prescott, aged 66, died March 12 of coronary occlusion.

Dr. Walter Monroe Matthews, Little Rock, aged 47, died May 2.

Dr. James Walter Walker, Fayetteville, aged 56, died May 4.

Dr. E. Burke Brown, Cotton Plant, aged 56, died May 6.

DISTRICT OF COLUMBIA

Dr. William Leneave Berkley, Washington, and Miss Charlotte Hamilton Priest were married April 11.

Deaths

Dr. George Frank Day, Washington, aged 78, died February 17 of pneumonia.

Dr. Francis M. Ward, Washington, aged 78, died recently of cerebral hemorrhage.

Dr. Leonard Lauriston Hardin, Washington, aged 66, died April 29 from a jejunal hemorrhage.

FLORIDA

The Alachua County Medical Society has elected the following officers for the coming year: Dr. Edwin H. Andrews, Gainesville, President; Dr. R. E. Summit, Gainesville, Vice-President; Dr. H. M. Merchant, Gainesville, Secretary-Treasurer.

The Polk County Medical Society has elected the following officers for the coming year: Dr. S. A. Clark, Lakeland, President; Dr. W. W. Shafer, Haines City, Vice-President; Dr. J. R. Boulware, Jr., Lakeland, Secretary-Treasurer.

Dr. James Maxey Dell, Gainesville, has been made Superintendent of the Florida Farm Colony for the Feebleminded, succeeding the late Dr. James H. Colson.

Dr. Julius C. Davis, Quincy, has been made a member of the State Board of Medical Examiners.

Dr. William H. Pickett has been made Director of the Escambia County Health Unit.

Dr. E. C. Swift and Dr. Ferdinand Richards, Jacksonville, have removed to the Greenleaf Building.

Dr. Osmah E. Harrel and Miss Margaret Jane Hughes, both of Jacksonville, were married April 6.

Deaths

Dr. Frank Doig Francis, Tampa, aged 57, died April 5 of cerebral hemorrhage, arteriosclerosis and nephritis.

Dr. George Edward Webb Hardy, Jr., Tampa, aged 43, died March 26 of cerebral and coronary thrombosis.

Dr. John B. Curtis, Orange Heights, aged 81, died March 4 of bronchopneumonia and peritonitis.

Dr. Theodore Frank Foster, Pensacola, aged 37, died February 10 of bilateral polycystic kidney and uremia.

Dr. James Edward Thompson, Miami Beach, aged 61, died recently of heart disease.

Dr. Harry Dash Johnson, Daytona Beach, aged 59, died recently.

Dr. John Mell Smith, Starke, aged 50, died March 3 of abscess of the liver.

Dr. Joseph N. Fogarty, Daytona Beach, aged 60, died May 5.

GEORGIA

Dr. George A. Traylor, Augusta, was made President-Elect of the Georgia State Medical Association at the annual meeting in Savannah April 24 and Dr. B. H. Minchew, Waycross, was installed as President.

The McDuffie County Medical Society has elected the following officers for the coming year: Dr. C. W. Churchill, Thomson, President; Dr. B. F. Riley, Jr., Thomson, Vice-President; Dr. J. R. Wilson, Thomson, Secretary-Treasurer.

The Worth County Medical Society has elected the following officers for the coming year: Dr. H. S. McCoy, Sylvester, President; Dr. J. L. Tracy, Sylvester, Vice-President; Dr. G. S. Sumner, Sylvester, Secretary-Treasurer.

The Telfair County Medical Society has elected the following officers for the coming year: Dr. S. T. Parkerson, McRae, President; Dr. W. H. Born, McRae, Vice-President; Dr. F. P. Harbin, Lumber City, Secretary-Treasurer.

The Ben Hill County Medical Society has elected the following officers for the coming year: Dr. G. W. Willis, Ocilla, President; Dr. J. E. McMillan, Fitzgerald, Vice-President; Dr. L. S. Osborne, Fitzgerald, Secretary-Treasurer.

The Elbert County Medical Society has elected the following officers for the coming year: Dr. J. E. Johnson, Sr., Elberton, President; Dr. W. A. Johnson, Elberton, Vice-President; Dr. A. S. Johnson, Elberton, Secretary.

The Laurens County Medical Society has elected the following officers for the coming year: Dr. O. H. Check, Dublin, President; Dr. A. T. Coleman, Dublin, Vice-President; Dr. R. G. Ferrell, Jr., Dublin, Secretary-Treasurer.

The Rockdale County Medical Society has elected the following officers for the coming year: Dr. P. J. Brown, Conyers, President; Dr. P. S. Smith, Conyers, Vice-President; Dr. H. E. Griggs, Conyers, Secretary-Treasurer.

The Toombs County Medical Society has elected the following officers for the coming year: Dr. J. E. Mercer, Vidalia, President; Dr. H. D. Youmans, Lyons, Vice-President; Dr. W. W. Odom, Lyons, Secretary-Treasurer.

The Dooly County Medical Society has elected the following officers for the coming year: Dr. H. A. Mobley, Vienna, President; Dr. M. L. Malloy, Vienna, Secretary-Treasurer.

The Terrell County Medical Society has elected the following officers for the coming year: Dr. Guy Chappell, Dawson, President; Dr. J. H. Lewis, Dawson, Vice-President; Dr. Steve P. Kenyon, Dawson, Secretary-Treasurer.

The Houston-Peach Counties Medical Society has elected the following officers for the coming year: Dr. J. W. Story, Perry, President; Dr. H. E. Evans, Perry, Vice-President; Dr. R. L. Cater, Perry, Secretary-Treasurer.

The Turner County Medical Society has elected the following officers for the coming year: Dr. H. M. Belflower, Sycamore, President; Dr. W. L. Story, Ashburn, Vice-President; Dr. J. H. Baxter, Ashburn, Secretary.

The Morgan County Medical Society has elected the following officers for the coming year: Dr. W. M. Fambrough, Bostwick, President; Dr. D. M. Carter, Madison, Vice-President; Dr. W. C. McGeary, Madison, Secretary-Treasurer.

The Meriwether County Medical Society has elected the following officers for the coming year: Dr. T. W. Jackson, Manchester, President; Dr. V. H. Bennett, Gay, Vice-President; Dr. R. B. Gilbert, Greenville, Secretary-Treasurer.

The Stephens County Medical Society has elected the following officers for the coming year: Dr. J. H. Terrell, Toccoa, President; Dr. E. F. Chaffin, Toccoa, Vice-President; Dr. C. L. Ayers, Toccoa, Secretary-Treasurer.

The Coweta County Medical Society has elected the following officers for the coming year: Dr. W. H. Tanner, Newnan, President; Dr. G. W. Hammond, Newnan, Vice-President; Dr. M. F. Cochran, Newnan, Secretary-Treasurer.

The Franklin County Medical Society has elected the following officers for the coming year: Dr. S. D. Brown, Royston, President; Dr. B. T. Smith, Carnesville, Secretary-Treasurer.

The Greene County Medical Society has elected the following officers for the coming year: Dr. E. G. Adams, Greensboro, President; Dr. Goodwin Gheesling, Greensboro, Secretary-Treasurer.

The Blue Ridge Medical Society has elected the following officers for the coming year: Dr. J. M. Daves, Blue Ridge, President; Dr. E. L. Prince, Morganton, Vice-President; Dr. C. B. Crawford, Blue Ridge, Secretary-Treasurer.

The Grady County Medical Society has elected the following officers for the coming year: Dr. A. B. Reynolds, Cairo, President; Dr. J. V. Rogers, Cairo, Secretary-Treasurer.

The Warren A. Candler Hospital, Savannah, has elected the following officers for the coming year: Dr. W. A. Cole, President; Dr. D. B. Edwards, Vice-President; Dr. J. L. Elliott, Secretary-Treasurer.

Dr. Calhoun McDougall, Atlanta, has been made a member of the Board of Directors of the Fulton National Bank.

Dr. Roy R. Kracke, Emory University, was installed as President of the American Society of Clinical Pathologists at the meeting of the Society in Kansas City, Missouri, recently.

Dr. W. L. Ballenger, Atlanta, has been made President of the Garden Hills Civic League.

Dr. R. S. O'Neal, LaGrange, has been made President of the University of Georgia School of Medicine Alumni Association.

Dr. Harry Ainsworth, Thomasville, has been made Secretary of the Atlantic Coast Line Surgeons' Association.

Dr. E. C. Harris has moved from Hawkinsville to Macon, where he opened offices in the Bibb Building.

Dr. J. F. Covington has moved from Cartersville to Canton.

Dr. J. H. Campbell has moved from Athens to Jefferson.

Dr. Clarence B. Palmer has moved from Rutledge to Covington and opened offices in the Star Building.

Dr. W. E. Thomasson has moved from Talbotton to Carrollton.

The Meriwether County Medical Society was recently entertained at dinner by Dr. R. B. Gilbert, Greenville.

DEATHS

Dr. Paul Plez Cooper, Alma, aged 46, died March 10 of heart disease.

Dr. Charles William Crane, Augusta, aged 61, died April 1.

Dr. Nichols Peterson, Tifton, aged 68, died March 13 of pneumonia.

Dr. William Clifton Lyle, Carrollton, aged 65, died April 15.

Dr. Robert Lee Miller, Waynesboro, aged 66, died March 31.

Dr. Jesse P. Prescott, Lake Park, aged 70, died recently.

Dr. James Meriwether Hull, Augusta, aged 77, died April 13.

Dr. William Henry Estes, Lincolnton, aged 59, died April 21.

Dr. John Monroe Sigman, Macon, aged 56, died April 10.

KENTUCKY

The Perry County Medical Society has elected the following officers for the coming year: Dr. Guy Pinckley, Anco, President; Dr. J. C. Coldiron, Hazard, Vice-President; Dr. D. D. Carr, Hazard, Secretary-Treasurer.

The Floyd County Medical Society has elected the following officers for the coming year: Dr. O. T. Stephens, Prestonburg, President; Dr. L. A. Donoho, Wayland, Vice-President; Dr. J. G. Archer, Prestonburg, Secretary-Treasurer.

DEATHS

Dr. Samuel P. Miller, Columbia, aged 71, died February 26.

Dr. Samuel Addison Taylor, Montpelier, aged 78, died recently of cerebral hemorrhage.

Dr. Leander O. Jones, Hebbardsville, aged 84, died February 18 of cerebral hemorrhage.

Dr. Latta Arthur Crandell, Lewisport, aged 46, died March 28 of lobar pneumonia.

LOUISIANA

Dr. Charles M. Horton, Franklin, was made President-Elect of the Louisiana State Medical Association and Dr. Hiram W. Kostmayer, New Orleans, was installed as President.

DEATHS

Dr. John A. McCorkle, Ponchatoula, aged 77, died March 8 of cerebral hemorrhage.

Dr. Joseph Bynum Stanley, Jackson, aged 54, died recently of cerebral thrombosis and bronchopneumonia.

MARYLAND

The University Hospital, Baltimore, had as guest speaker before a recent meeting Dr. Walter Bauer, Boston, Massachusetts.

Dr. Nicholas Floyd Adams, Jr., and Miss Margaret Bardelle Roberts, both of Baltimore, were married April 24.

DEATHS

Dr. Tilghman Brice Marden, Preston, aged 66, died March 17 of diabetes mellitus.

Dr. Frances E. Brown, Catonsville, aged 69, died March 9.

MISSISSIPPI

Dr. William L. Little, Wesson, was made President-Elect of the Mississippi State Medical Association and Dr. Harvey F.

Continued on page 22

Facts you should know about RIPE BANANAS

Easily digested — Non-irritating — Good source of food energy, vitamins, minerals — Pleasant taste

RIPE BANANAS are an easily digested bland food which supplies essential vitamins and minerals, and is popular with most people. They are non-irritating . . . do not ferment easily in the intestines . . . and create intestinal conditions unfavorable to the growth of putrefactive bacteria.

The carbohydrates of a ripe banana comprise about 22% of its total weight when peeled. They consist chiefly of a mixture of sugars—sucrose, dextrose, and levulose—which are readily absorbed, even by infants and young children with gastro-intestinal disturbances.

Besides being an excellent source of food energy, bananas are a good source of Vitamins A, B, C, and G, contribute to the diet important minerals and yield alkaline mineral residues in the body. With their soft fiber, pectins, high content of sugars, low content of protein and fat, and their vitamins, bananas seem adapted to act as a normalizer of colonic functioning.

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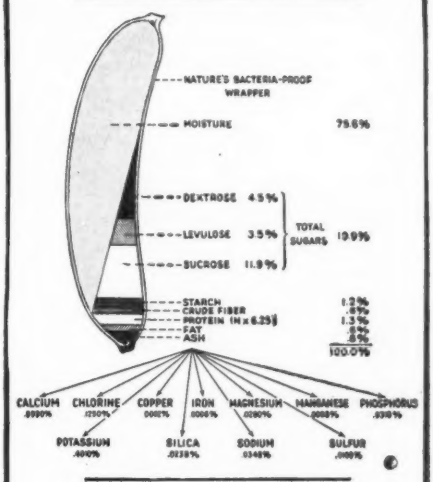
Bananas ripen naturally at room temperature. If they are partially ripe when purchased—i.e., in the green-tipped stage—they should be kept at comfortable room temperature (never in the refrigerator) until the pulp has softened and the skin is golden yellow flecked with brown. That is when they're fully ripe and at their very best in flavor.

Proximate Chemical Composition of Fully Ripe Bananas



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S. M. J., 7-36

Continued from page 774

Garrison, Sr., Jackson, was installed as President at the meeting in Greenville May 4.

The Mississippi State Pediatric Society held its annual meeting in Greenville May 5-7.

DEATHS

Dr. Edwin Cyril Gillespie, Lambert, aged 45, died February 22 of pneumonia.

Dr. Henry S. Gully, Meridian, aged 76, died recently of pneumonia.

Dr. Hugh Moran Anderson, Sanatorium, aged 55, died February 6.

Dr. Philip Beekman, Natchez, aged 71, died February 4 of cerebral thrombosis and arteriosclerosis.

MISSOURI

Dr. Dudley S. Conley, Columbia, was made President-Elect of the Missouri State Medical Association at the annual meeting in Columbia and Dr. Ross A. Woolsey, St. Louis, was installed as President.

Dr W. McKim Marriott, St. Louis, has resigned as Dean of the Washington University School of Medicine, a position he has held since 1923, to accept the position of Dean of the School of Medicine, University of California, Berkeley-San Francisco.

Dr. Theodore R. Meyer, Paw Paw, has been made Health Officer of St. Louis County.

Rev. Alphonse M. Schwitalla, S.J., Ph.D., Dean, St. Louis University School of Medicine, St. Louis, has been made President of the North Central Association of Colleges and Secondary Schools.

Dr. Robert L. Tolle, St. Louis, and Miss Mary Virginia Murphy were married recently.

DEATHS

Dr. Herman Fred Koestering, Kansas City, aged 72, died February 22 of pyloric obstruction and postoperative pneumonia.

Dr. Charles Hodge Wallace, Jr., St. Joseph, aged 36, died April 26 following a mastoid operation.

Dr. Thomas L. Duckett, Lamar, aged 81, died February 23 of thrombosis.

Dr. William D. Delzell, Springfield, aged 91, died recently.

Dr. Thomas S. Watson, Bevier, aged 78, died recently of angina pectoris.

Dr. Albert Anderson Long, Kansas City, aged 65, died recently of sarcoma of the femur.

Dr. Alvis Taylor Marshall, Wyatt, aged 56, died February 6 of cirrhosis of the liver.

Dr. Edward Frazer Herndon, Kansas City, aged 85, died February 22 of pneumonia.

Dr. A. C. Heidman, Columbia, aged 74, died March 3 of influenza and pulmonary edema.

Dr. William A. Powers, Pacific, aged 59, died March 11 of Hodgkin's disease.

Dr. Harry S. P. Lare, St. Louis, aged 74, died March 8 of cerebral hemorrhage.

Dr. William H. Mallory, Joplin, aged 57, died March 15.

Dr. Austin McMichael, Rock Port, aged 81, died April 7.

Dr. John W. Good, Fordland, aged 65, died May 11 of heart disease.

NORTH CAROLINA

Dr. Wingate M. Johnson, Winston-Salem, was made President-Elect of the Medical Society of North Carolina at the annual meeting in Asheville May 6.

Dr. William P. Murphy, Boston, Massachusetts, lectured at Duke University, Durham, May 7.

Dr. William J. Dieckmann, Chicago, Illinois, and Dr. Edward R. Baldwin, Saranac Lake, New York, were speakers before the students and staff of Duke University, Durham, recently.

DEATHS

Dr. James Thomas A. Wright, Salisbury, aged 63, died March 10 of pneumonia.

Dr. James Albert Anderson, Gastonia, aged 59, died March 13 of nephritis and myocarditis.

Dr. William H. Hughes, Greensboro, aged 73, died February 17 of basal fracture of the skull due to a fall down the stairs.

Continued on page 24

THE NEW YORK POLYCLINIC

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Continued from page 22

Dr. Mary E. Lapham, Highlands, aged 75, died recently of heart disease.

Dr. T. H. Higgins, Trap Hill, aged 62, died April 13.

OKLAHOMA

Dr. Samuel A. McKeel, Ada, was made President-Elect of the Oklahoma State Medical Association at the meeting in Enid and Dr. George R. Osborn, Tulsa, was installed as President.

Dr. R. B. Ford, Holdenville, has returned from abroad, where he took postgraduate work.

Dr. J. H. Plunkett, Wagoner, is taking postgraduate work in Nashville, Tennessee.

Deaths

Dr. Thomas Moore Hoskins, Oklahoma City, died February 8.

Dr. Greene B. Jackson, Fairland, aged 72, died March 25 of carcinoma of the stomach.

SOUTH CAROLINA

Dr. Julius H. Taylor, Columbia, was made President-Elect of the South Carolina Medical Association at the meeting recently in Greenville and Dr. Robert C. Bruce, Greenville, was installed as President.

Dr. Gordon R. Westrope, Columbia, has been made Health Officer of Cherokee County.

Dr. John Y. O'Daniel, formerly of Erwin, Tennessee, has been made Health Officer of Marlboro County.

Dr. Edward P. White, Gaffney, has been made Health Officer of Richland County.

Dr. William Burns Jones, Columbia, has been made Health Officer of Chester and Union Counties.

Deaths

Dr. Bartolo Pedro Oliveros, Charleston, aged 75, died March 2 of cerebral hemorrhage.

Dr. Ruth B. Carroll, Columbia, aged 46, died recently of cerebral hemorrhage.

Dr. Julian Terrell Coggeshall, Darlington, aged 60, died March 1 of pneumonia.

Dr. James Monroe Austin, Columbia, aged 38, died recently.

TENNESSEE

The Tennessee State Pediatric Society has elected the following officers for the coming year: Dr. John M. Lee, Nashville, President; Dr. W. L. Rucks, Memphis, Vice-President; Dr. Kinsey M. Buck, Memphis, Secretary-Treasurer.

The Tennessee Academy of Ophthalmology and Otolaryngology has elected the following officers for the coming year: Dr. R. O. Rychener, Memphis, President; Dr. H. Carroll Smith, Nashville, Vice-President Dr. W. D. Stinson, Memphis, Secretary-Treasurer.

The Tennessee Valley Medical Association and Postgraduate Assembly met in Knoxville June 10-12.

The Davidson County Medical Society had as guest speaker at a recent meeting Dr. Andrew A. Eggston, New York, New York.

Deaths

Dr. John Harvey Carr, Maynardville, aged 63, died February 27.

Dr. Peter Eckel Walker, Gallatin, aged 92, died February 28 of bronchopneumonia.

Dr. Harry Edgar Hall, Chattanooga, aged 44, died recently of cerebral hemorrhage.

Dr. Isaac L. McGinness, Pikeville, aged 64, died February 27.

Continued on page 26

Classified Advertisements

FLORENCE ANNAN CARPENTER, medical translator, abstractor and writer, announces her removal to 1801 Sixteenth St., N.W., Washington, D. C., where she will be able to give her clients the benefits of the Surgeon General's Library.

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St. Louis, Mo. St. Paul, Minn.
Dallas, Texas

Continued from page 24

TEXAS

The San Patricio-Aransas-Refugio Counties Medical Society has elected the following officers for the coming year: Dr. W. S. Noble, Aransas Pass, President; Dr. G. E. Glover, Austwell, Vice-President; Dr. F. S. Ewing, Sinton, Secretary.

The Memorial Hospital Staff, Quanah, has elected the following officers for the coming year: Dr. J. J. Hanna, President; Dr. J. W. Conley, Vice-President; Dr. Mildred Hanna, Secretary.

The Masonic Hospital Staff, El Paso, has elected the following officers for the coming year: Dr. Wickliffe R. Curtis, Chief of Staff; Dr. Chester D. Awe, Vice-Chief; Dr. Delphin von Briesen, Secretary.

The Mercy Hospital Staff, Brownsville, has elected the following officers for the coming year: Dr. O. V. Lawrence, President; Dr. R. H. Eisaman, Vice-President; Dr. John S. Peak, Secretary.

The Central Texas District Society has elected the following officers for the coming year: Dr. J. E. Robinson, Temple, President; Dr. J. E. Lattimore, Waco, Secretary.

Dr. Robert J. Jaehne, Austin, has been made Health Officer of Travis County.

Dr. Charles D. Lipscomb, Quitman, has been made Health Officer of Wood County.

Dr. S. W. Holley has been made Assistant Professor of Pathology at the University of Texas School of Medicine, Galveston, to succeed Dr. J. W. Williams, resigned.

Dr. John S. Cooper has been made City Health Officer of Greenville to succeed Dr. Benjamin F. Arnold.

Dr. Victor E. Schulze, San Angelo, has been made a Fellow in the American College of Physicians.

Dr. Charles S. Carter, Bells, has been made a member of the State Board of Medical Examiners.

Dr. Edythe Hershey, Dallas, has been made Director of Child Health and Maternity Divisions of the State Health Department.

Dr. O. R. O'Neill, Paris, is taking postgraduate work in New York.

Dr. R. M. Bellamy, Pampa, has returned after taking postgraduate work in Rochester, Minnesota.

Dr. J. L. Bressler, formerly of Chicago, has located in Houston for the practice of ophthalmology and otolaryngology.

Dr. Clyde Adams has moved from Henderson to Rusk.

Dr. P. C. Anders has moved from Lockney to Longview.

Dr. Ira F. Brake has moved from Jacksonville to San Augustine.

Dr. Oren H. Chandler has moved from Hamilton to Ballinger.

Dr. Charles M. Cole has moved from Bedias to Navasota.

Dr. John A. Cook has moved from Asherton to Cotulla.

Dr. Bert E. Davis has moved from Dallas to Denton.

Dr. D. W. Dunn has moved from Nocona to Fort Washakie, Wyoming.

Dr. James Edgar Goodnight has moved from San Antonio to Pearsall.

Dr. W. J. Graber has moved from Navasota to Beaumont.

Dr. J. P. Haley has moved from Warren to C. C. C. Camp, Bogata.

Dr. W. Calvin Jones has moved from Wellington to Pampa.

Dr. W. Leggett has moved from Fostoria to Cleveland.

Dr. Harold Lindley has moved from Colorado to Pecos.

Continued on page 28

The Ella Oliver Home

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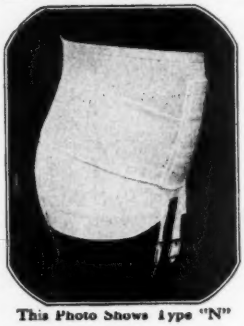

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Continued from page 26

Dr. T. L. Morgan has moved from Hereford to Lubbock.
Dr. Don C. Peterson has moved from Flint, Michigan, to Austin.
Dr. R. C. L. Robertson has moved from Snyder to New York, New York.
Dr. L. E. Silverthorn has moved from Bonham to Paris.
Dr. E. F. Tritt has moved from Bastrop to Temple.
Dr. Ann West has moved from Wilson to Dallas.
Dr. R. B. Wolford has moved from Bonham to Wichita Falls.

Deaths

Dr. James Daniel Blevins, Beaumont, aged 54, died March 8 of pneumonia.
Dr. Henry C. Amos, Denton, aged 51, died March 26 of lobar pneumonia.
Dr. Davis Benjamin Beach, Hamilton, aged 52, died March 18.
Dr. Marquis E. Daniel, Honey Grove, aged 69, died March 9 of coronary embolism.
Dr. Hardin Davenport Irvan, Gladewater, aged 52, died March 9 of injuries received in an automobile accident.
Dr. Crittendon E. Keller, San Antonio, aged 87, died March 2 of arteriosclerosis and senile dementia.
Dr. Cuthbert Lynn Hosmer, Houston, aged 59, died recently of uremia, arteriosclerosis and nephritis.
Dr. Thomas H. D. Stuart, Dallas, aged 96, died February 22 of nephritis.
Dr. Samuel Donaldson, Petros, aged 59, died March 2 of cerebral hemorrhage.
Dr. Frank Bozeman King, Houston, aged 72, died March 16 of angina pectoris.
Dr. William Anthony Cooper, Sindom, aged 79, died recently.
Dr. Junius Ambrose Rawlings, El Paso, aged 70, died March 23.
Dr. Walter Homer Moses, Georgetown, aged 61, died March 1 of pneumonia.
Dr. Joseph C. Waterman, Catarina, aged 76, died recently.
Dr. John Chauncey Van Nuys, Lufkin, aged 67, died March 12 of pneumonia.
Dr. J. L. Ball, Cleburne, aged 95, died March 5.
Dr. Reuben Bennett Anderson, Seguin, aged 76, died March 17.

VIRGINIA

The Virginia Academy of Science has elected the following officers for the coming year: Dr. H. E. Jordan, University, President; Dr. E. C. L. Miller, Richmond, Secretary-Treasurer.

The South Piedmont Medical Society has elected the following officers for the coming year: Dr. J. W. Devine, Lynchburg, President; Dr. Ernest G. Scott, Lynchburg, Dr. Roy W. Upchurch, Danville, Dr. L. P. Bailey, Nathalie, Dr. W. R. Martin, Charlotte, Vice-Presidents; Dr. J. A. Owen, South Boston, Secretary-Treasurer.

The Amelia County Medical Society has elected the following officers for the coming year: Dr. G. Craig Eggleston, Amelia, President; Dr. G. A. Arhart, Amelia, Vice-President; Dr. J. L. Hamner, Mannboro, Secretary-Treasurer.

The Roanoke Academy of Medicine has elected the following officers for the coming year: Dr. Fred E. Hamlin, President;

Continued on page 32

The "MESCO" Laboratories manufacture the largest line of Ointments in the world. Sixty different kinds. We are originators of the Professional Package. Specify "MESCO" when prescribing ointments. Send for lists.

Manhattan Eye Salve Co.
LOUISVILLE, KENTUCKY

Diarrhea in Infancy

Take It In Time

Just a day or two of light nourishment prepared from Mellin's Food as suggested below will usually avert an intestinal disturbance that might develop into a serious diarrhea if not taken in hand at the first appearance of loose stools.

Mellin's Food*. . . 4 level tablespoonfuls

Water (boiled, then cooled) . . . 16 ounces

Give one to three ounces every hour or two until the stools lessen in number and improve in character.

The mixture may then be strengthened by the gradual substitution of boiled skimmed milk for water until the quantity of skimmed milk is equal to the normal quantity of milk used in the baby's formula. Finally the fat of the milk may be gradually replaced by skimming less and less cream from the milk.

Samples sent to physicians upon request.

Directions for using Mellin's Food are left entirely to the physician.

Mellin's Food Company, Boston, Mass.

**MELLIN'S FOOD: Produced by an infusion of Wheat Flour, Wheat Bran and Malted Barley admixed with Potassium Bicarbonate — consisting essentially of Maltose, Dextrins, Proteins and Mineral Salts.*

Picnic Poisoning—

"PICNIC POISONING"—a gastro-intestinal symptom-group particularly prevalent on Mondays, characterized by symptoms of diarrhea, mild enteritis, flatulence and general abdominal discomfort.

HISTORY—a picnic, outing, or other occasion where large and varied amounts of food and drink were consumed with little regard to normal rules of diet.

TREATMENT—usually consists of elimination of the toxic, irritating material without irritation to the inflamed intestinal mucosa.... Kaomagma adsorbs intestinal toxins and soothes the inflamed mucosa. Being fluid, it mixes with the intestinal content, forming a soft mass easily evacuated without interference with normal digestion.

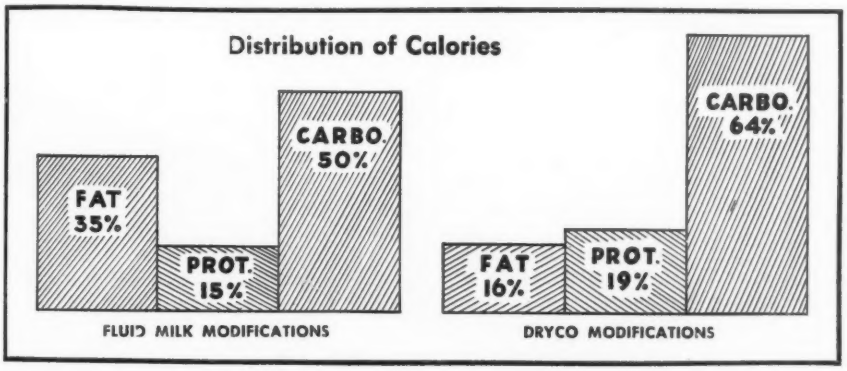
Kaomagma Plain and Kaomagma with Mineral Oil supplied in 12-oz. bottles.

When the thermometer soars!

"It is probably wise to avoid formulas with high fat"...Holt & McIntosh
Diseases of Infancy and Childhood
ed.10, New York, 1933
Appleton-Century, p. 186

● A prolonged hot spell decreases the infant's digestive capacity, and diarrhea often follows. Effective safeguards against summer upsets are clean milk (Dryco is safe!) and a decrease in the fat content of the formula.

During the summer months many physicians turn to Dryco modifications for infant feeding. Compare the distribution of calories in a Dryco formula with commonly-used fluid milk modifications.



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SUSTAINING, EASILY DIGESTED, DELICIOUS

They are uniquely useful—

As a light lunch whenever tired or hungry.

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Soothing to the throat, after tonsillectomy.

Always a beneficial confection in place of harmful sweets.

Now at your druggists in handy pocket flasks—10c

Also, in larger sizes

Natural and Chocolate Flavors

HORLICK'S MALTED MILK CORP.

Racine, Wis.

Continued from page 28

Dr. H. H. Wescott, Dr. T. J. Hughes, Vice-Presidents; Dr. J. M. Bishop, Secretary-Treasurer.

Dr. Dudley C. Smith, University, has been made President of the Charlottesville Rotary Club.

Dr. Kenneth F. Maxcy, University, has been made Professor and Head of the Department of Preventive Medicine at the University of Minnesota Medical School, Minneapolis.

Dr. A. L. Carson, Jr., Fairfax, has been made Assistant to Dr. B. B. Bagby in the State Department of Health, Bureau of Child Health.

Dr. J. M. Holloway, Fredericksburg, has been made President of the Rotary Club of that city.

The Medical College of Virginia, Richmond, had as guest speakers recently Dr. Carl L. A. Schmidt, San Francisco, California, and Dr. W. O. Fenn, Rochester, New York.

The University of Virginia Medical Society had as guest speaker at the meeting on May 7 Dr. Albert M. Snell, Rochester, Minnesota.

Dr. Arnold R. Rich, Baltimore, delivered the Alpha Omega Alpha Lecture at the University of Virginia Department of Medicine, Charlottesville.

Dr. Charles A. Young, Roanoke, has returned after taking postgraduate work abroad.

Dr. R. S. Herring, Richmond, has returned after taking postgraduate work in Vienna.

Dr. Beverly L. Holaday, formerly of Charlottesvile, has located at Suffolk.

Dr. William R. Pretlow, formerly of The Plains, has located in Warrenton.

Dr. W. S. Cox, formerly of Shacklefords, has located in West Point.

Dr. F. T. Hauser, formerly of Fort Monroe, has located at Purcellville.

Dr. William T. Pyles, formerly of Roanoke, has located at Franklin.

Dr. Grey C. Hughes, formerly of Boston, Massachusetts, has located at Martinsville.

Continued on page 34

says Sophocles...
"SLEEP IS THE PHYSICIAN OF PAIN"
CIBA
"Ciba"
Dial, "Ciba", is available in tablets · powder · ampules · elixir. Request sample and literature.
Dial, "Ciba", brings serene and refreshing sleep... to guard the irritated nervous system against further damage from lack of slumber. Thus, the patient's mental and physical states are benefited—nature is aided in the task of healing.
Dial—diallylmalonylurea—is quickly effective in much smaller doses than barbital, U.S.P. It is rapidly eliminated and in therapeutic doses exerts no injurious action on respiration or circulation.
Indications—As a hypnotic, Dial, for relief of insomnia; suggested dose 1 to 3 tablets. As a sedative, ¼ to ½ tablet.
Each Dial Tablet contains 1½ grs., approximately 0.1 Gm.
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Atabrine is supplied in tablets of 0.1 Gm. (1½ grains), with groove for division, in tubes of 15 and bottles of 500.

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Continued from page 32

Dr. Delmar J. Weaver, Jr., Madison, and Miss Beulah Borah Thrift were married April 2.

Dr. Walter L. Thomas, Jr., Lynchburg, and Miss Maisie Denhold were married March 10.

Dr. Elam C. Toone, Jr., Richmond, and Miss Adelaide Salter were married April 11.

Deaths

Dr. Walter White Burgess, Roanoke, aged 28, died March 16 of pneumonia.

Dr. Clarence Linden Lewis, Jr., Richmond, aged 71, died recently of angina pectoris.

Dr. Newton Eugene McDannald, News Ferry, aged 75, died May 4.

Dr. William Edwards Croxton, West Point, aged 54, died May 9 of pneumonia.

Dr. Thomas R. Marshall, Wan, aged 64, died recently of coronary occlusion.

Dr. Callie P. Capps, Meherrin, aged 68, died May 14.

WEST VIRGINIA

The Preston County Medical Society has elected the following officers for the coming year: Dr. A. V. Cadden, Hopemont, President; Dr. D. J. Rudasill, Kingwood, Vice-President; Dr. C. Y. Moser, Kingwood, Secretary-Treasurer.

The Harrison County Medical Society had as guest speaker at a recent meeting Dr. Austin I. Dodson, Richmond, Virginia.

The Cabell County Medical Society had as guest speaker at a recent meeting Dr. Hugh G. Beatty, Columbus, Ohio.

Deaths

Dr. William E. Talbot, Harrisville, aged 77, died in February of complications due to a fractured hip received in a fall.

Dr. Alton Sanford, Weston, aged 31, died recently of pneumonia.

Dr. Anna Laura Taylor, Elkins, aged 70, died March 9 of gangrene.

Dr. Albert Lee Coffield, New Martinsville, aged 50, died February 26 of cardiorenal disease.

Dr. Russell Felts Hufford, Welch, aged 28, died May 19.

Pancreas Therapy
BY
Oral Administration

An aid in the decreased capacity of the patient in states of pancreatic deficiency.

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As adjuvant therapy, the oral administration of Pyridium often brings prompt relief of the distressing symptoms which frequently accompany urethritis. Shortening of the duration of treatment and reduction of the number of instances in which complications develop have been reported.

When local treatment is indicated, the use of Pyridium solution may be effectively combined with the oral administration of the tablets. The preparation is non-toxic and non-irritative in therapeutic doses.

Pyridium is available in tubes of 12 and bottles of 50 (0.1 gram) tablets; 1% solution in 100 cc. bottles; powder in 2, 5, and 10 gram bottles; and 1% jelly in 1 oz. collapsible tubes. Descriptive literature will be sent upon request.

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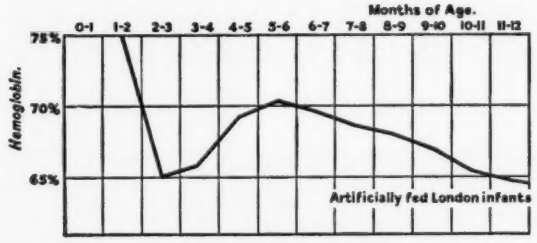
Nutritional Anemia in Infants



Hemoglobin level in the blood of infants of various ages. Note fall in hemoglobin, which is closely parallel to that of diminishing iron reserve in liver of average infant. Chart adapted from Mackay. It is possible to increase significantly the iron intake of the bottle-fed from birth by feeding Dextri-Maltose With Vitamin B in the milk formula. After the third month Pablum offers substantial amounts of iron for both breast- and bottle-fed babies.

Reasons for Early Pablum Feedings

1. The iron stored in the infant's liver at birth is rapidly depleted during the first months of life. (Mackay,[1] Elvehjem.[2])

2. During this period the infant's diet contains very little iron—1.44 mg. per day from the average bottle formulae of 20 ounces, or possibly 1.7 mg. per day from 28 ounces of breast milk. (Holt.[3])

For these reasons, and also because of the low hemoglobin values so frequent among pregnant and nursing mothers (Coons,[4] Galloway[5]), the pediatric trend is constantly toward the addition of iron-containing foods at an earlier age, as early as the third or fourth month. (Blatt,[6] Glazier,[7] Lynch[8].)

The Choice of the Iron-Containing Food

1. Many foods reputed to be high in iron actually add very few milligrams to the diet because much of the iron is lost in cooking or because the amount fed is necessarily small or because the food has a high percentage of water. Strained spinach, for instance, contains only 1 to 1.4 mg. of iron per 100 gm. (Bridges.[9])

2. To be effective, food iron should be in soluble form. Some foods fairly high in total iron are low in soluble iron. (Summerfeldt.[10])

3. **Pablum is high both in total iron (30 mg. per 100 gm.) and soluble iron (7.8 mg. per 100 gm.) and can be fed in significant amounts without digestive upsets as early as the third month, before the initial store of iron in the liver is depleted. Pablum also forms an iron-valuable addition to the diet of pregnant and nursing mothers.**

Pablum (Mead's Cereal thoroughly cooked and dried) consists of wheatmeal, oatmeal, cornmeal, wheat embryo, brewers' yeast, alfalfa leaf, beef bone, iron salt and sodium chloride.

[1-10] Bibliography on request.

MEAD JOHNSON & COMPANY, Evansville, Indiana, U. S. A.

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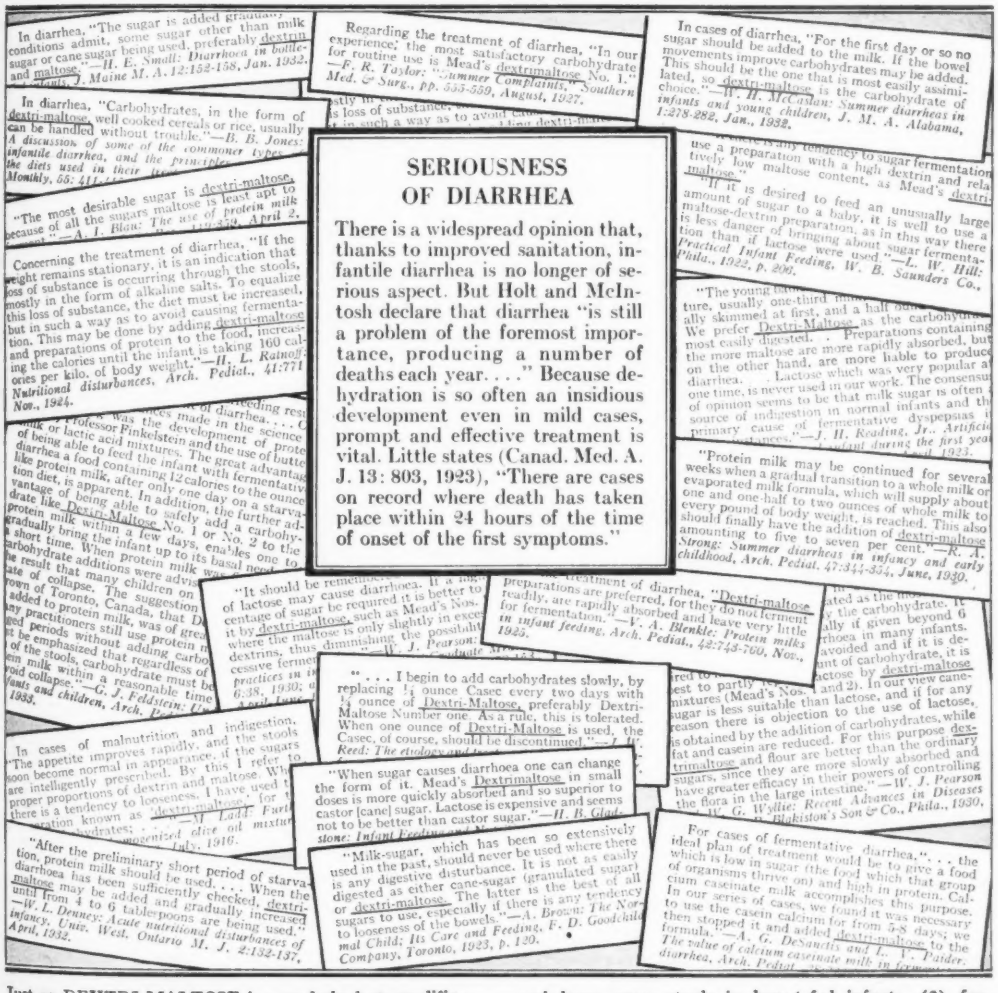
DIARRHEA

"the commonest ailment of infants in the summer months"

(HOLT AND McINTOSH: HOLT'S DISEASES OF INFANCY AND CHILDHOOD, 1933)

One of the outstanding features of DEXTRI-MALTOSE is that it is almost unanimously preferred as the carbohydrate in the management of infantile diarrhea.


In diarrhea, "The sugar is added gradually ... conditions admit, some sugar other than milk sugar or cane sugar being used, preferably dextrin and maltose."—H. E. Smalll: Diarrhoea in bottle-fed infants, J. Maine M. A. 14:152-158, Jan. 1932.
In diarrhea, "Carbohydrates, in the form of dextri-maltose, well cooked cereals or rice, usually can be handled without trouble."—B. B. Jones: A discussion of some of the commoner types of infantile diarrhea, and the principles underlying the diets used in their treatment, Wisconsin Monthly, 55: 411-414, 1916.
"The most desirable sugar is dextri-maltose, because of all the sugars maltose is least apt to ..."—A. J. Blau: The use of protein milk ... April 2, ...
Concerning the treatment of diarrhea, "If the weight remains stationary, it is an indication that loss of substance is occurring through the stools, mostly in the form of alkaline salts. To equalize this loss of substance, the diet must be increased, but in such a way as to avoid causing fermentation. This may be done by adding dextri-maltose and preparations of protein to the food, increasing the calories until the infant is taking 160 calories per kilo. of body weight."—H. L. Ranoff: Nutritional disturbances, Arch. Pediat., 41:771 Nov., 1924.
Regarding the treatment of diarrhea, "In our experience, the most satisfactory carbohydrate for routine use is Mead's dextrimaltose No. 1."—F. K. Taylor: "Summer Complaints," Southern Med. & Surg., pp. 555-559, August, 1927.
In cases of diarrhea, "For the first day or so no sugar should be added to the milk. If the bowel movements improve carbohydrates may be added. This should be the one that is most easily assimilated, so dextri-maltose is the carbohydrate of choice."—H. H. McCaslan: Summer diarrheas in infants and young children, J. M. A. Alabama, 1:278-282, Jan., 1932.
SERIOUSNESS OF DIARRHEA
There is a widespread opinion that, thanks to improved sanitation, infantile diarrhea is no longer of serious aspect. But Holt and McIntosh declare that diarrhea "is still a problem of the foremost importance, producing a number of deaths each year. . . ." Because dehydration is so often an insidious development even in mild cases, prompt and effective treatment is vital. Little states (Canad. Med. A. J. 13: 803, 1923), "There are cases on record where death has taken place within 24 hours of the time of onset of the first symptoms."
use a preparation with a high dextrin and relatively low maltose content, as Mead's dextri-maltose."
"If it is desired to feed an unusually large amount of sugar to a baby, it is well to use a maltose-dextrin preparation, as in this way there is less danger of bringing about sugar fermentation than if lactose were used."—L. W. Hill: Practical Infant Feeding, W. B. Saunders Co., Phila., 1923, p. 206.
"The young ... ture, usually one-third ... ally skimmed at first, and a half ... We prefer Dextri-Maltose as the carbohydrate most easily digested. . . . Preparations containing the more maltose are more rapidly absorbed, but on the other hand, are more liable to produce diarrhea. . . . Lactose which was very popular at one time, is never used in our work. The consensus of opinion seems to be that milk sugar is often a source of indigestion in normal infants and the primary cause of fermentative dyspepsias ..."—J. H. Reading, Jr.: Artificial ... infant during the first year ..., 1923.
"Professor Finkelstein and the development of protein milk, after only one day on a starvation diet, is apparent. In addition, the further advantage of being able to safely add a carbohydrate like Dextri-Maltose No. 1 or No. 2 to the protein milk within a few days, enables one to gradually bring the infant up to its basal needs in a short time. When protein milk was advised ... carbohydrate additions were advised ... the result that many children on ... rate of collapse. The suggestion ... town of Toronto, Canada, that ... added to protein milk, was of great ... any practitioners still use protein ... ged periods without adding carbo ... t be emphasized that regardless of ... of the stools, carbohydrate must be ... em milk within a reasonable time ... oad collapse."—G. J. Feldstein: Diseases of Infants and Children, Arch. Pediat., ... 1933.
"Protein milk may be continued for several weeks when a gradual transition to a whole milk or evaporated milk formula, which will supply about one and one-half to two ounces of whole milk to every pound of body weight, is reached. This also should finally have the addition of dextri-maltose amounting to five to seven per cent."—R. A. Strong: Summer diarrheas in infancy and early childhood, Arch. Pediat. 47:344-354, June, 1930.
"It should be remembered ... of lactose may cause diarrhea. It is better to ... centage of sugar be required it is better to ... it by dextri-maltose, such as Mead's Nos. ... where the maltose is only slightly in excess ... dextrins, thus diminishing the possibility ... cessive fermentation ..."—W. J. Pearson: ... practices in ... 6:38, 1930; ... April, ...
"... preparations are preferred, for they do not ferment readily, are rapidly absorbed and leave very little for fermentation."—V. A. Blenkle: Protein milks in infant feeding, Arch. Pediat., 42:743-760, Nov., 1925.
"... I begin to add carbohydrates slowly, by replacing ½ ounce Casec every two days with ½ ounce of Dextri-Maltose, preferably Dextri-Maltose Number one. As a rule, this is tolerated. When one ounce of Dextri-Maltose is used, the Casec, of course, should be discontinued."—J. ... Reed: The etiology and ...
"When sugar causes diarrhoea one can change the form of it. Mead's Dextrimaltose in small doses is more quickly absorbed and so superior to castor [cane] sugar. Lactose is expensive and seems not to be better than castor sugar."—H. B. Gladstone: Infant Feeding and ...
"Milk-sugar, which has been so extensively used in the past, should never be used where there is any digestive disturbance. It is not as easily digested as either cane-sugar (granulated sugar) or dextri-maltose. The latter is the best of all sugars to use, especially if there is any tendency to looseness of the bowels."—A. Brown: The Normal Child; Its Care and Feeding, F. D. Goodchild Company, Toronto, 1923, p. 120.
In cases of malnutrition and indigestion, "The appetite improves rapidly, and the stools soon become normal in appearance, if the sugars are intelligently prescribed. By this I refer to proper proportions of dextrin and maltose. Wh ... there is a tendency to looseness, I have used ... dextri-maltose ... for ... ration known as ... dextrin and maltose ... —M. Ladd: Further ... carbohydrates; ... modified olive oil mixtur ... Pediat., July, 1916.
"After the preliminary short period of starvation, protein milk should be used. . . . When the diarrhoea has been sufficiently checked, dextri-maltose may be added and gradually increased until from 4 to 6 tablespoons are being used."—W. L. Denney: Acute nutritional disturbances of infancy, Univ. West. Ontario M. J. 2:132-137, April, 1932.
For cases of fermentative diarrhea, ". . . the ideal plan of treatment would be to give a food which is low in sugar (the food which that group of organisms thrive on) and high in protein. Calcium caseinate milk accomplishes this purpose. In our series of cases, we found it was necessary to use the casein calcium for from 5-8 days; we then stopped it and added dextri-maltose to the formula."—A. G. DeSanctis and I. ... Patiden: The value of calcium caseinate milk in ... diarrhea, Arch. Pediat. ...

Just as DEXTRI-MALTOSE is a *carbohydrate* modifier of choice, so is CASEC (calcium caseinate) an accepted *protein* modifier. Casec is of special value for (1) colic and loose green stools in breast-fed infants, (2) fermentative diarrhea in bottle-fed infants, (3) prematures, (4) marasmus, (5) celiac disease.

When requesting samples of Dextri-Maltose, please enclose professional card to cooperate in preventing their reaching unauthorized persons.

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MAPHARSEN

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The outstanding feature of Mapharsen is its rapidly beneficial effect upon early syphilis. Disappearance of spirochetes occurs promptly. Healing of lesions is rapid and complete. Symptomatic improvement is most satisfactory. Positive Wassermann reactions are reversed in a large percentage of cases.

Over half-a-million injections of Mapharsen have been administered without any serious accident—no death has occurred following its use; serious nitritoid crisis has not been reported. Although mild cases of dermatitis may occur, the incapacitating exfoliative type is very rarely encountered. Reactions observed are usually of a mild nature; a slight reduction in the dose will ordinarily prevent recurrence.

Mapharsen is an efficient antisyphilitic agent—a distinct refinement in arsenical therapy.

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